American Journal of Diseases of Children

VOLUME 37 MARCH, 1929 NUMBER 3

TYPES OF BODY BUILD IN INFANTS*

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Within the past sixty years marked progress has been made in the understanding of the environmental factors in the etiology of disease. But great though the advances have been, the fact that persons react differently to the same sort of trauma, bacterial, mechanical, chemical or psychologic, has kept alive the concept of constitution as a factor in the etiology and course of disease. Prior to 1870, though some progress had been made in the study of the individual, the term constitution had been widely used to designate factors, the exact nature of which was unknown, and it was only natural that, with the discovery of the facts of bacteriology and immunology, research should be directed toward these more promising fields and that the term constitution should become largely discredited. In America, where the traditional background is almost entirely lacking and where experimental medicine on a large scale is of comparatively recent origin, this subject was almost entirely ignored. Within the past few years, however, the clinical study of the individual as a factor in disease has been revived. The introduction of more accurate methods of study has already yielded results, not only of great general biologic interest, but of immediate clinical importance as well.

Constitution as a factor in the etiology and course of diseases of infants has been the subject of a study at Bellevue Hospital during the past three years. For purposes of simplification the various aspects of the individual constitution such as sex, body build and race (black or white) have been studied separately.

Sex, as an important factor in diseases of infants, has long been recognized.[1] Boys die in much larger proportion during the first year

* Submitted for publication, Aug. 4, 1928.

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* Read before the Section on Diseases of Children at the Seventy-Ninth Annual Session of the American Medical Association at Minneapolis, June 15, 1928.

1. Clarke, J.: Observations on Some Causes of the Excess of Mortality of Males Above That of Females, Phil. Tr. Roy. Soc., London **16**:122, 1786.

of life than do girls (134 to 100, U. S. Birth Registration Area, 1924). The younger the child, the higher is this proportion. Of great interest is the fact that the hypersusceptibility of the male may be influenced by environmental factors.[2] The winter season, residence in urban communities, and the English and Welsh climates in comparison with the American tend to have an unfavorable effect on the male infant.

It is the purpose of the present paper to describe various types of body build in infants, and to note briefly some of their disease associations.

TYPES OF BODY BUILD IN ADULTS

That persons differ according to their type of body build is an ancient observation taught by Hippocrates. In 1902, Manouvrier,[3] by careful observation and accurate measurement, was able to demonstrate that there are two predominant types of body build among European adults, an observation which has been confirmed by numerous workers since that time. In America, work along these lines has been particularly active (Goldthwaite,[4] Bryant,[5] Mills,[6] Bean,[7] Stockard,[8] Draper[9]), but until recently little attention had been given to this subject by the clinician.

These two predominant types of body build among European adults have been variously named by different authors. The terminology introduced by Stockard,[8] a linear and a lateral type, are simple and as descriptive as any, and will be used throughout this paper. The descriptions of the body types of adults given subsequently are taken largely from the papers by Stockard.

The linear type adult is distinguished by a long head, a high narrow nasal bridge, sharp prominent nose, narrow mouth arch with teeth that are usually ill set, small poorly developed lower jaw, a long thin neck, high square angular shoulders, long slender extremities, slender bones and muscles, a short trunk tapering to the waist and a narrow intercostal angle. The stomach is vertically placed and long and narrow, the

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2. Bakwin, H.: The Sex Factor in Infant Mortality, Human Biology, to be published.

3. Manouvrier: Mém. Soc. d'anthropologie de Paris, 1902, vol. 2, pt. 3.

4. Goldthwaite, J. E.: An Anatomic and Mechanistic Conception of Disease, Boston M. & S. J. **172**:881, 1915.

5. Bryant, J.: The Carnivorous and Herbivorous Types of Man, Boston M. & S. J. **170**:795, 1914; **172**:321, 1915; **173**:384, 1915.

6. Mills, R. W.: The Relation of Bodily Habitus to Visceral Form, Position, Tonus and Mortality, Am. J. Roentgenol. **4**:155, 1917.

7. Bean, R. B.: The Two European Types, Am. J. Anat. **31**:359, 1923.

8. Stockard, C. R.: Human Types and Growth Relations, Am. J. Anat. **31**: 261, 1923.

9. Draper, G.: Human Constitution, Philadelphia, W. B. Saunders Company, 1924.

intestines are short and active. The liver is small and more vertical than in the lateral type of person. The skin is thin, as is the epithelial lining of the alimentary tract. Persons of the linear type of body build tend to be underweight.

The lateral type of adult is the opposite of the linear. The head is broad, the nasal bridge wide and low, the palatal arch broad and low and the teeth smoothly set. The lower jaw is prominent and strong, the neck is short and large, the shoulders rounded and sloping, and the extremities not long but stocky. The bones are large, and the muscles are heavy. The trunk is long and full and bulging at the waist, and the intercostal angle is obtuse. The stomach and intestines are long and sluggish. Persons of the lateral type tend to be overweight.

Personality make-up is determined to a considerable extent by the type of body build.[10] Such qualities as idealism, egoism, fastidiousness, pedantry, moodiness and cynicism are characteristic of the linear type of person, while talkativeness, good humor, and plodding perseverance belong to the lateral type.

BODY TYPE IN INFANTS

An attempt to classify infants according to their body build was made by Lederer[11] in 1923. He divided them into the four groups described by Sigaud:[12] the muscular type, with strongly developed musculature, round head, broad shoulders and large chest; the digestive type, with small nose, depressed at the base, large mouth, broad lower jaw and large abdomen; the respiratory type with broad nose and large chest; the cerebral type with large head, narrow shoulders and chest, and long narrow fingers. His paper contains many interesting observations and is important in that it represents the first attempt to study body type in normal infants. Unfortunately, the scheme of classification used (Sigaud) is open to criticism, since it lacks the anatomic basis essential for a sound anthropomorphic classification.

Schultz[13] has shown that the individual characteristics of man appear early in fetal life. Such bodily features as the shape of the nose, the relation between the upper and lower jaws, the shape of the hand, the relative length of the limbs, vary fully as much and often more in fetuses than in adults. Asymmetry between the right and left halves of the body are also distinguishable early in fetal life. The right humerus is longer than the left in the same proportion of instances as in adults.

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10. Kretschmer, E.: Körperbau und Charakter, Berlin, Julius Springer, 1922.
11. Lederer, R.: Konstitutionspathologie in den medizinischen Spezialwissenschaften, vol. 1, Berlin, Julius Springer, 1924.
12. Sigaud, C.: La forme humaine, 1914.
13. Schultz, A.: Fetal Growth of Man and Other Primates, Quart. Rev. Biol. **1**:465 (Oct.) 1926.

So, also, the left foot is larger in fetuses in the same proportion as in adults. Asymmetry in the size of the ear occurs more often in fetuses than in adults. Negro fetuses may be distinguished from white as soon as the human form is recognizable, and the criteria for differentiation are practically identical with those in adult life.

Method of Study.—The data used in this study were obtained from the examination of sixty male infants ranging from 2 weeks to 14 months of age, the majority of whom were well. Since these observations will be reported more fully at a later time, it will suffice here merely to state rather than describe in detail the methods used. In addition to the usual medical history and physical examination, anthropometric measurements, corresponding to those in use in adults, were made. Measurements of infants are difficult because of the relative indistinctness of the bony points and the lack of cooperation of the patient. Since the absolute measurements are much smaller than in adults, the percentage of error is correspondingly larger. Throughout our work we have taken cognizance of these sources of error. Roentgenograms of the long bones and chests, and in a few instances of the stomach, were also made. A plaster cast of the palate was made in each patient. Whenever possible, postmortem measurements of the size of the stomach and length of the intestine were made, and the organs were weighed.

As in European adults, so in infants, two predominant types of body build may be distinguished. The linear type infant has a long narrow head, long face, small lower jaw, high narrow nasal bridge, narrow palate often pointed anteriorally, long thin neck, small chest circumference in comparison with the head, narrow shoulders and hips, and long tapering fingers with long nails often showing lunulae. Roentgenologically, the chest is narrow and long, only slightly larger below than above. The diaphragm is sloping, and the long axis of the heart is almost vertical. Infants of the linear type of body build tend to be underweight.

The lateral type infant has a round head, a short face with large lower jaw, a low, broad nasal bridge, broad palate, rounded anteriorally, short large neck, large chest, broad shoulders and hips, and short stubby fingers with short nails. Roentgenologically, the chest widens out markedly below, the diaphragm is transverse and the long axis of the heart is almost transverse. Infants of the lateral type of body build tend to put on weight easily.

Some of these type differences are illustrated in the accompanying figures. Figure 1 (*a*) shows a male infant, 6 days old, whose birth weight was 2,550 Gm. The infant shown in figure 1 (*b*) is a male whose birth weight was 4,560 Gm. The differences between the two infants are striking. In contrast to figure 1 (*b*) the face shown in figure 1 (*a*) is long and narrow (facial index[14] 71 in comparison with

14. Facial index $= \frac{\text{Facial Height}}{\text{Facial Diameter}} \times 100.$

61 for the infant shown in 1 (*b*)), the nasal bridge is high, the neck is long and thin and the chest and hips are narrow. Similar differences are apparent between the two babies shown in figure 2.

Variations in Palatal Shape in Infants.—Variations in the shape of the palate of infants are illustrated in figure 3. All the impressions

Fig. 1.—Types of body in infants. (*a*) Linear type of male infant, 6 days old, birth weight, 2,550 Gm.; (*b*) lateral type of male infant, birth weight, 4,560 Gm.

were taken during life from infants under 3 months of age. The palatal impression shown in figure 3 (*a*) is long, narrow and pointed anteriorly. It was obtained from an extremely thin girl infant, 2 months old. The impression shown in figure 3 (*d*) is broad and rounded

anteriorly. It was obtained from a boy, 1 month old. The other two palates represent intermediate types. A series of palates obtained from infants between 6 and 8 months of age are shown in figure 4.

Variations in Shape of Hand in Infants.—In figure 5 are illustrated the various types of the shape of the hand observed in infants. The

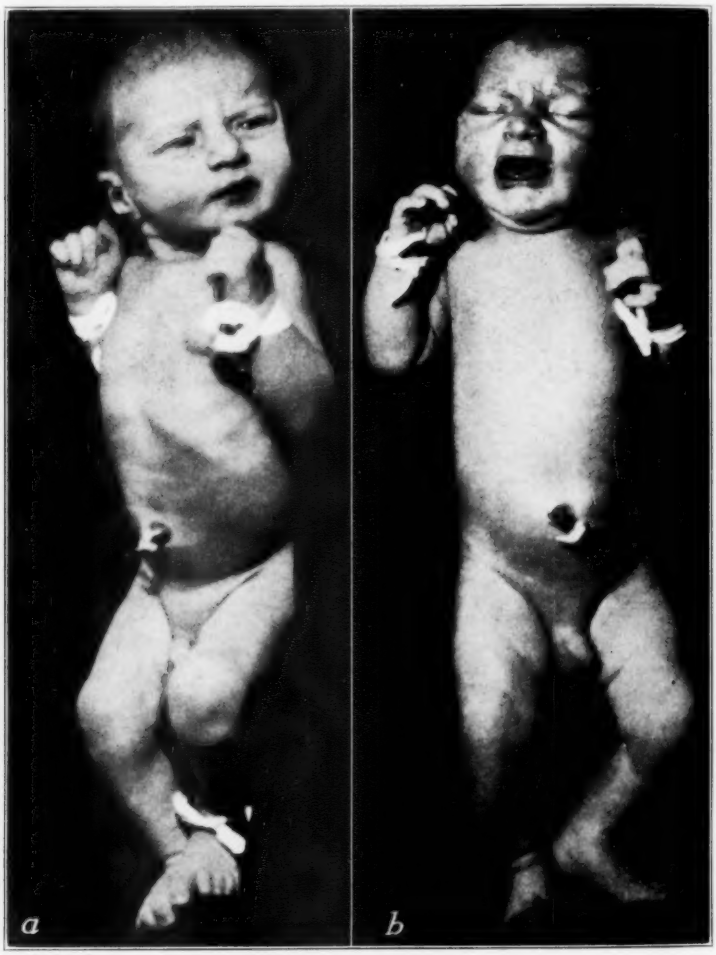

Fig. 2.—Types of body build in infants. (*a*) Linear type infant; (*b*) lateral type infant.

long tapering fingers with the long nails in figure 5 (*a*) differ strikingly from the short stubby fingers with the short, broad nails in figure 5 (*d*).

Variations in Shape of Chest and Heart in Infants.—It is not our purpose to discuss all the types of heart shadows seen in infants.

These have been described in a paper by De Buys and Samuel.[15] We wish here merely to point out that the infant shows variations in the shape of the heart similar to those observed in adults and that, like in adults, these variations correspond in a general way to the type of body build.

The shape of the mediastinal contents of infants has been shown by Gerstenberger [16] to vary markedly with the phase of respiration. During expiration the mediastinal contents appear much wider than during inspiration. This is particularly true for the upper mediastinal shadow,

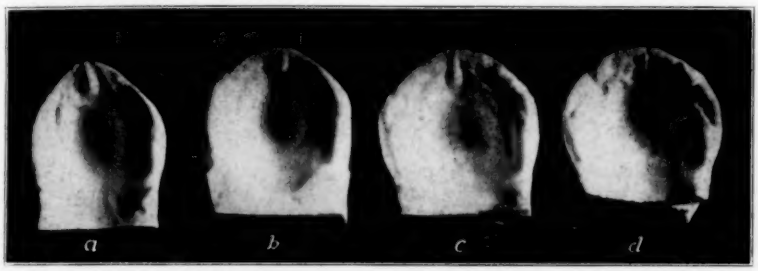

Fig. 3.—Variations in the shape of the hard palate of infants under 3 months of age. There is a gradation from the long, narrow, pointed palate on the left (*a*) to the short, broad, rounded palate on the right (*d*).

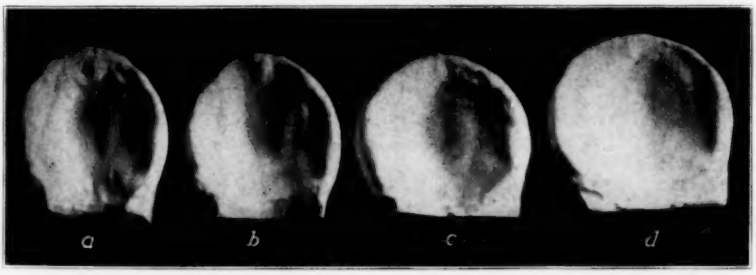

Fig. 4.—Variation in the shape of the hard palate of infants between 6 and 8 months of age. The same differences are apparent as in the younger infants.

but not nearly to the same degree for the cardiac shadow. Difference in the shape of the heart of infants is shown in figure 6. Figure 6 (*a*) is a long, narrow heart resembling the "hyposthenic" heart described by Hirsch and Shapiro [17] in their discussion of types of heart in adults.

15. De Buys, L. R., and Samuel, E. C.: Shadows in the Thorax of the Newly Born, Am. J. Dis. Child. **24**:397 (Nov.) 1922.

16. Gerstenberger, H. J.: The Factor of the Position of the Diaphragm in Roentgen-Ray Diagnosis of Enlarged Thymus, Tr. Am. Pediat. Soc. **32**:160, 1920.

17. Hirsch, I. S., and Shapiro, L. L.: The Morphology of the Heart in Relation to Habitus, and a New Method of Estimating Morphological Changes, Am. J. M. Sc. **162**:892 (Dec.) 1921.

and by Lincoln [18] in children. Figure 6 (*d*) shows a broad heart corresponding to the "hypersthenic" heart of Hirsch and Shapiro (Lincoln type D). Types (*b*) and (*c*) are intermediate forms.

In figure 7 are illustrated differences in the thickness of bone in infants. The two sets of bones of the forearm were taken from two infants each 1 month old. The radii are of exactly the same length, but the bones on the right are obviously thicker than those on the left.

Mixed types occur in infants as in adults, but usually one type of body build predominates in every person.

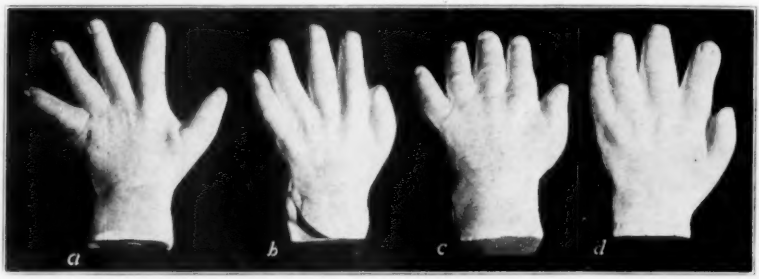

Fig. 5.—Variations in the shape of the hands in infants. (*a*) Long, narrow hand of linear type infant; (*b*)-(*c*) intermediate types of hands; (*d*) short hand with stubby fingers of lateral type infant.

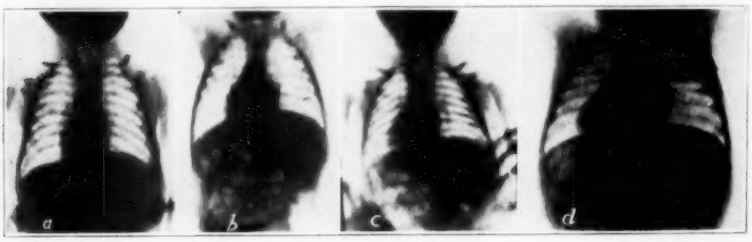

Fig. 6.—Variations in shape of chest and heart in infants. The plate on the left (*a*) is a long, narrow chest scarcely wider below than above, the diaphragm sloping sharply downward toward the periphery. The heart is elongated and thin and almost vertically placed. The chest plate on the right (*d*) is a marked contrast. The chest is short and broad and flares markedly below. The ribs, as well as the diaphragm, are almost transverse. The long axis of the heart is almost horizontal.

CLINICAL APPLICATIONS OF RESULTS OF STUDY

Three disease groups, malnutrition, tetany and eczema, were selected for study of body build. The same method of procedure was followed

18. Lincoln, E. M., and Spielman, R.: Studies on the Hearts of Normal Children, Am. J. Dis. Child. **35**:791 (May) 1928.

as for the group of well infants. Indexes for the three groups of patients are compared in the table. It will be seen that, as a group, the infants with malnutrition have proportionately narrower heads, longer faces, smaller lower jaws, narrower palates, narrower shoulders and hips than do the infants with eczema. The infants with tetany form an intermediate group, more nearly approximating the babies with eczema. Tetany is much more common in the lateral than in the linear type

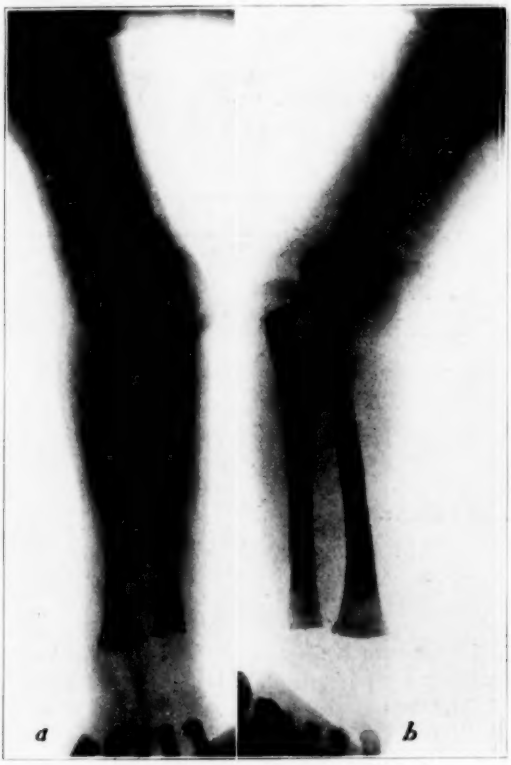

Fig. 7.—Variations in the thickness of bones in infants. The radii illustrated in the figures are of exactly the same length and belong to infants of the same age (1 month). The bones on the right are considerably thicker than those on the left.

infant. This indicates a physiologic difference in the calcium regulatory mechanism between the two groups of subjects and corresponds to the clinical impression that rickets and tetany occur more commonly in well nourished than in undernourished children.

SUMMARY AND CONCLUSIONS

1. In infants, as in adults, two predominant types of body build may be distinguished, a linear and a lateral.

2. The criteria for type differentiation appear to be largely similar to those in adults.

3. Infants suffering from malnutrition tend to be of the linear type of body build, infants with eczema of the lateral type, while tetanic infants form an intermediate group more nearly approaching the lateral type of body build.

4. A prominent characteristic of body type in infants as in adults is the nutritional state. The recognition of the type of body build is, from this point of view, of greater significance than in adults because of the importance of the nutritional state in the infant's physiology.

Median Indexes for Infants in Three Disease Groups

	Diagnosis		
	Median Index Values		
Index	Malnutrition	Tetany	Eczema
Cephalic breadth Cephalic length	82	84	87
Facial breadth Facial height	69	66	66
Infradentale mentum Nasal pros	56.5	59.5	61
Nasal breadth Nasal height	87	92	90
Chest circum. Head circum	90	94	97.5
Chest circum. Stature	59	63	62
Biacromial diameter Stature	21	22	23
Biiliac diameter Stature	15	17	16

DISCUSSION

DR. HENRY J. GERSTENBERGER, Cleveland: It is well that we have had evidence presented that constitution is of importance in the development of the disease and in the forming of symptoms of disease. It is well to bring back in this way the pendulum from the extreme position in which it was put by the influence of the bacterial era which was developed by Pasteur. However, I feel it also should be kept in mind that this may be overemphasized, and that there is definite danger that the pendulum may swing in the opposite direction and to an extreme end. The statement, for instance, that the author made regarding tetany and rickets, is, I think, fundamentally wrong. I think it is true that well nourished infants develop rickets and tetany, but they do not have rickets and tetany because they are of a peculiar constitution, but because they are growing well and being liberally fed. I do not think that constitution plays an important rôle in the development of rickets and tetany, nor in the development of scurvy or beriberi. Every infant and every animal will develop scurvy, rickets and beriberi if conditions are established which are fundamentally essential to the production of these conditions; for instance, the absence of sunlight in rickets.

It is true that men who work with animals, for instance, rats, find that in every group of rachitic rats there will be individual differences. All guinea-pigs too will

develop scurvy under proper conditions; however, there will be some little difference in the type of scurvy produced. Nevertheless, all guinea-pigs will develop scurvy and all rats rickets if the protective factors are withheld. Then, too, the habits of living and of working influence the general make-up and appearance of human beings. I beg to call your attention to the fact that physicians are usually recognized as a group. It has been shown that meat eaters have larger and more numerous capillaries, and that vegetable eaters or relatively poor meat eaters have smaller capillaries and fewer capillaries, and therefore are pale. I think it is a good illustration of the fact that food and working habits seem to influence the external appearance of the human being.

Dr. Tobias L. Birnberg, St. Paul: As one advances in the study of pediatrics, one enjoys watching the progress that has been made, and the swinging of the pendulum. We have continually swung the pendulum from one extreme to the other. We have had strong dilutions, and finally have fallen on concentrations. By this process of education, we are getting the proper dilution. We have changed our ideas along the line of fats. We used to feed high fat mixtures, and we found the danger of extreme feeding of fat mixtures, then we fed fat-free mixtures and now we are changing back to the feeding of moderate amounts of fat. The same thing occurred in carbohydrates. First there was a generous use of carbohydrates, then a fear of carbohydrates and now we are back to the high carbohydrates again. Years ago we spoke about types or constitutions. The old physicians, before the teaching of pathology and bacteriology was pronounced, spoke of these types as the thin, neuropathic, or linear type and the phlegmatic or lateral type. There is no question but that these two types do exist, but I want to warn about the danger of making a diagnosis of these types without first tending to establish the proper nutrition in these patients, and then making the final diagnosis of the type, because one must realize that these types have probably resulted from inheritance, and inheritance is merely the accumulation of many, many environments. We can try by present environment to change the effect of inheritance to make a distinct type. For example, the so-called neuropathic and linear type of person is thin because he has increased peristalsis, interference with secretions. If we take this thin, neuropathic type and build him up by giving him a high protein and high salt diet, like buttermilk, as Finkelstein long ago suggested, he will soon change to the lateral type. I also want to mention a few words on the other type, the exudative type which was mentioned. I do not believe the exudatives are usually of the thick type. Finkelstein showed there are two types of exudatives, the thin type and the thick type.

We have found from experience that by environment, special dietetic influence, we can change the two types of exudation infants. We can take the thin type and add salts and proteins to the diet and build them up. They will become the thicker type. We can take the thick type and give them a diet low in salts, low in proteins and low in water, and there will be a tendency for these subjects to become the thin type. By doing that it is remarkable the change that occurs in the individual. Not only the physical change but the change in his metabolism causes improvement in his exudative manifestations.

About tetany: Is the patient with tetany a thick type because thick types make tetany, or is it the results of the metabolism toward tetany? I believe that the tetany type of person, being low in calcium, naturally would have greater absorption of water in the tissues, and naturally would have a tendency toward the broad, thick type. If the amount of sodium-potassium salts can be decreased, the mechanic symptoms will disappear at once. Therefore, I think that the patient with tetany is thick because of his metabolism and not that he has tetany because he is thick.

DR. HARRY BAKWIN, New York: I did not intend to bring up constitution as the cause of any disease. As a matter of fact, I feel that disease is a resultant of a multiplicity of different factors only one of which is constitution. It has seemed to me that this factor has received too little emphasis. Dr. Gerstenberger fears the pendulum will swing too far in the direction of constitution. As far as I know, this is the first paper on constitution in infants that has been read before this section for some time. For a little while at any rate, there appears to be no danger that the constitutional factor in diseases of infants will be overemphasized. I was much interested in the remarks on tetany. The statement was made that both rickets and tetany are entirely dependent for their development on environmental factors. But the constitutional factor, sex, plays an important part in determining the incidence of tetany in infants, as shown by the fact that tetany occurs about twice as often in boys as in girls. As far as observations on animals are concerned, Dr. Charles Stockard has recently shown (AM. J. DIS. CHILD. **36**:310 [Aug.] 1928) that rickets is much more common in male dogs than in female dogs. As far as choice of profession and body build are concerned, although this is a subject unrelated to the present discussion, I think there is a distinct connection. The tailor and the longshoreman are distinctly different types.

THE VALUE OF DIFFERENT TYPES OF GLASS FOR TRANSMITTING ULTRAVIOLET LIGHT*

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Sufficient data are now available to show conclusively that irradiation with ultraviolet light is of positive benefit in the treatment of rickets. Frequently it is desirable to use sunlight as a source of ultraviolet rays, but in winter months, in this latitude, it is often necessary to use sunlight that has passed through glass. Accordingly, an investigation was undertaken to determine the extent to which ultraviolet light passed through different types of glass readily obtainable on the open market. The investigation was conducted along two lines: A study was made with rachitic children to determine the therapeutic value of sunlight that passed through different types of glass, and a second study was made with albino rats to secure additional data concerning the pathologic condition of the bones and their mineral content.

The results obtained by treating rachitic children with sunlight which had passed through different types of glass formed the subject of an earlier paper.[1] The present paper reports the results obtained from the second study.

EXPERIMENTAL WORK

Source of Ultraviolet Light.—As sunshine does not provide uniform amounts of ultraviolet light from day to day, a Cooper-Hewitt Uviarc lamp was employed as a source of ultraviolet light. For the purpose of this study, it was decided to record the current available and the amount of current actually utilized by the lamp. Accordingly, four readings daily were made of the voltage and amperage of the current in the line and that in the arc. An average was taken of these readings, and the daily wattage thus obtained is reported in figure 1. As figure 1 discloses, the wattage of both the arc and the line varied

* Submitted for publication, Aug. 23, 1928.

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1. Wyman, E. T.: Boston M. & S. J. **197**:376 (Sept. 8) 1927.

decidedly from day to day. Studies of ultraviolet light for its antirachitic value ordinarily do not record its intensity. It is impossible, therefore, to judge whether or not the intensity of the ultraviolet light used in these experiments is comparable to that used by other investigators.

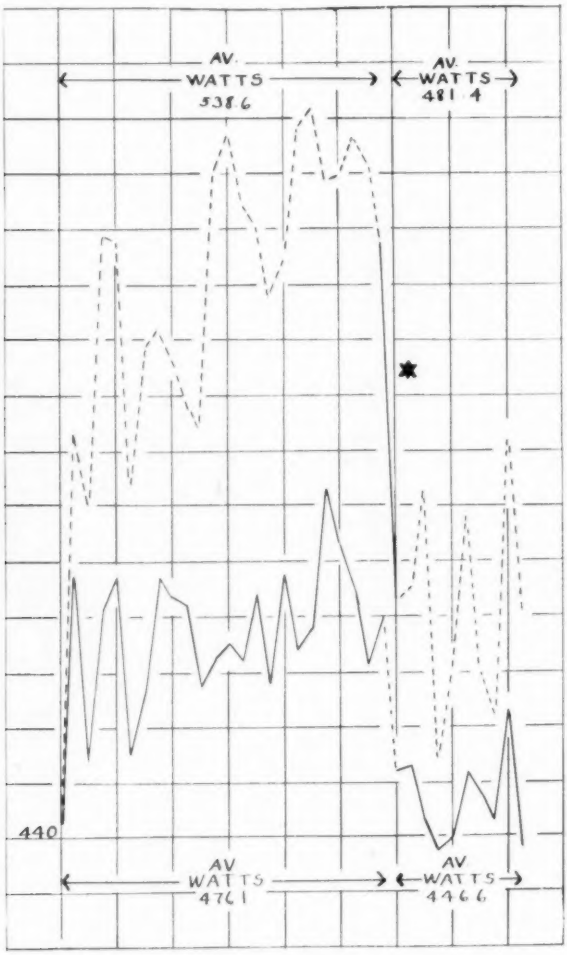

Fig. 1.—Curve representing the daily variation in wattage of a Cooper-Hewitt Uviarc lamp. The dotted line represents the wattage of the line; the solid line, that of the arc; the star, changed line leads to higher voltage points in auxillary. Each horizontal division indicates a period of four days, each vertical division, 10 watts.

Method of Irradiation.—The therapeutic value of ultraviolet light varies inversely as the square of the distance of the animals which are being irradiated from the lamp producing the ultraviolet light. It is

essential, therefore, that this distance remain the same throughout the period of irradiation. The animals used in this experiment were subjected to irradiation at a distance of 3 feet for fifteen minutes daily. The cages illustrated in figure 2 were devised for this study to keep the animals at a definite distance from the lamp during irradiation. Since the cages were only 2 inches (5 cm.) high, the animals could not vary their distance from the light during the period of irradiation. The center of each cage was 36 inches (91.44 cm.) from the center of the quartz tube containing the mercury vapor arc. Each day, all the cages were moved one space around the hexagon in which they were

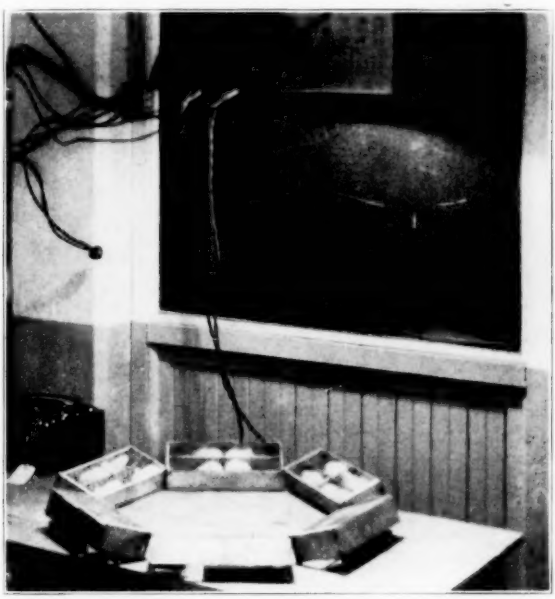

Fig. 2.—Method of irradiating animals.

grouped. At the end of six days, each cage had occupied all sides of the hexagon, and during the experimental period, it had rotated around the hexagon nearly six times. The amount of irradiation, accordingly, was exactly the same for all the cages.

Nature of the Glass.—The glasses selected for this study were window glass obtained from a hardware store, Corex glass obtained from the Corning Glass Works of Corning, N.Y., and Vitaglass "Cathedral" obtained from the Vitaglass Company. A wire screen which permitted the passage of practically all the ultraviolet light was used as a control.

Corex glass, which is superior to all other glasses yet produced and rivals quartz in transparency, in the spectral region of 260 to 300 mm.,

transmits from 91.4 to 91.8 per cent of the total number of ultraviolet solar rays absorbed by window glass. Vitaglass, an English product, transmits from 50 to 60 per cent of the total number of ultraviolet solar rays absorbed by ordinary window glass.

The results of tests of the transparency of the glasses used are shown in the spectrogram (fig. 3). It will be seen that the Corning glass transmitted rays down to 265 millimicrons and the Vitaglass down to 290 millimicrons, the extreme limit of the spectrum of the sun. Of the two samples of ordinary window glass, one transmitted rays down to 312 millimcrons and the other to 333 millimicrons.

Laboratory Procedure.—The study was conducted on a prophylactic basis and was of five weeks' duration. The animals, which were 32

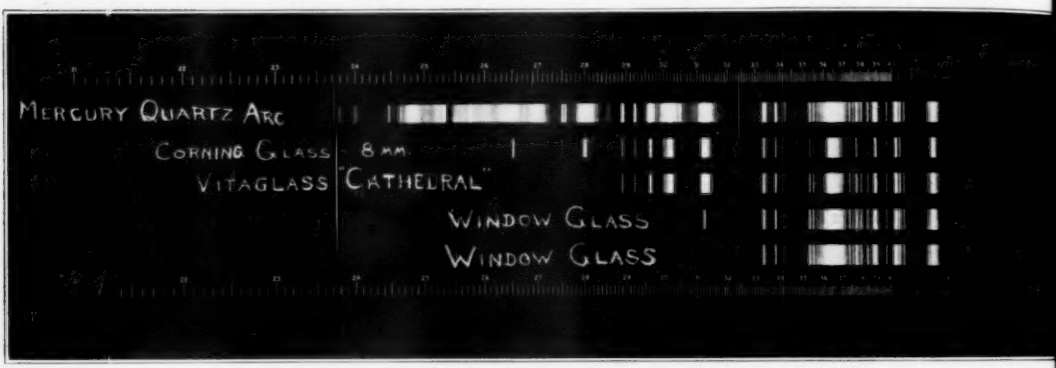

Fig. 3.—Spectrogram showing relative transparency of Corning glass, Vitaglass, "cathedral" and window glass.

days old when the experiment began, were fed a diet (Steenbock) consisting of 76 per cent yellow corn (ground), 20 per cent wheat gluten, 3 per cent calcium carbonate and 1 per cent sodium chloride.

The animals were so selected as to form five groups as nearly alike as possible. These groups were designated "controls," "window," "Corning," "Vitaglass" and "direct irradiation." The therapeutic value of the ultraviolet light that passed through the screens was judged by: the increase in weight of the animals during the experiments, and in the calcium and phosphorus content of the blood; roentgenograms of the femur and tibia; pathologic examination of the femur and tibia, and the ash content of these bones at the end of the experiment.

Records of Growth.—The increase in the weight of the animals during the experimental period is shown in figure 4. The curves represent the individual animals and the composite curves and dotted line show the average increase of body weight computed for each group. In a comparison of the gain in growth of the animals in the different

groups during the period of the experiments, it will be noted that the animals in the control group gained slightly less than 50 Gm. in weight. The animals which were irradiated under window glass also gained slightly less than 50 Gm. The average gain in weight for the animals in the Corning and the direct irradiation groups was identical, and that of the Vitaglass group slightly less. This would indicate that little, if any, ultraviolet light passed through the window glass, whereas the Corning glass and Vitaglass transmitted enough ultraviolet light to cause the animals to gain practically as much in weight as those which received direct irradiation.

Calcium and Phosphorus Content of Blood.—As a group rather than an individual formed the basis for the comparison of the anti-

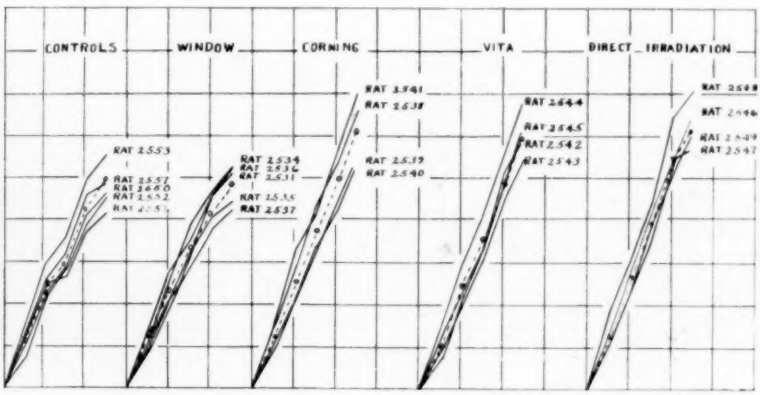

Fig. 4.—Increase in weight of the animals during the experiment. The solid line represents the growth of the individual animals; the composite dotted and solid line the average growth of the group. Each horizontal division indicates a period of two weeks, each vertical division, 10 Gm.

TABLE 1.—*Amount of Calcium and Phosphorus in Blood Serum*

	Control Group, per Cent	Window Group, per Cent	Corning Group, per Cent	Vitaglass Group, per Cent	Direct Irradiation Group, per Cent
Calcium	10.2	9.0	11.2	11.1	11.8
Phosphorus	3.7	2.4	5.7	4.9	5.4
Product of calcium and phosphorus	37.7	21.6	63.8	54.4	63.7

rachitic activity of ultraviolet light that has passed through various screens, the blood obtained from the animals of each group was pooled. The calcium [2] and phosphorus [3] content of the serum was determined by the usual laboratory method. The results obtained are given in table 1.

It will be noted (table 1) that the number of milligrams of calcium and phosphorus per hundred cubic centimeters of blood serum, for the

2. Kramer, B., and Tisdall, F. F.: J. Biol. Chem. **47**:475, 1921.
3. Fiske, C. H., and Subbarow, Y.: J. Biol. Chem. **56**:375, 1925.

animals in the control group and for those irradiated through window glass, indicates that the animals in both groups were decidedly rachitic; whereas the same sort of evidence for the groups of animals irradiated through the Corning glass and Vitaglass shows these animals to be normal. The animals irradiated through Corning glass apparently received more protection than those irradiated through Vitaglass and about the same as those receiving direct irradiation.

Roentgenograms.—Roentgenograms [4] were made of the right hind leg of the animals at the termination of the experiment. Figure 3 shows the extent of calcification of the femur and tibia of the animals in the control group; figures 4, 5, 6 and 7 supply the same evidence for the animals in the window glass, Corning glass, Vitaglass and direct irradiation groups respectively.

Fig. 5.—Roentgenogram of animals of control group.

The roentgenograms show that the animals of the control and window groups were decidedly rachitic. On the other hand, those of the Corning group and direct irradiation group did not show any discernible rickets. The animals in the Vitaglass group showed a line of diminished calcification between the diaphysis and the epiphysis of the tibia, indicating a mild degree of rickets.

Pathology.—In the examination of histologic material from the animals the same plan was utilized as that reported in a previous paper.[5] The animals were numbered, and no intimation of the particular treatment they had received was given to the pathologist until the data were

4. Roentgenograms were made by Edward C. Vogt, M.D., roentgenologist for the Children's and Infants' Hospital, Boston.

5. Wyman, E. T.; Holmes, A. D.; Smith, L. W.; Stockbarger, D. C., and Pigott, M. G.: Am. J. Dis. Child. **34**:753 (Nov.) 1927.

approved and assembled. Identical sections were made through the femur and tibia of representative animals from each group. The degree of rachitic change was graded on a 1, 2, 3, 4 basis: Grade 1 represented the normal; grade 4, the typical marked rickets as expressed by the

Fig. 6.—Roentgenogram of animals of window glass group.

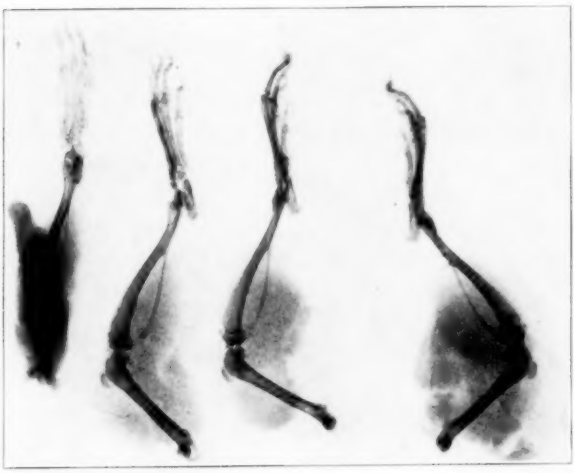

Fig. 7.—Roentgenogram of animals of Corning glass group.

control animals, and grades 2 and 3, two intermediate stages of rickets, early and moderately advanced.

There were five groups. The first consisted of control animals on the experimental rickets producing diet. These animals were not

irradiated, and their bones presented the typical histologic picture of rickets. They were placed in grade 4.

The second group consisted of animals on the same diet and irradiated through ordinary window glass. These animals at autopsy

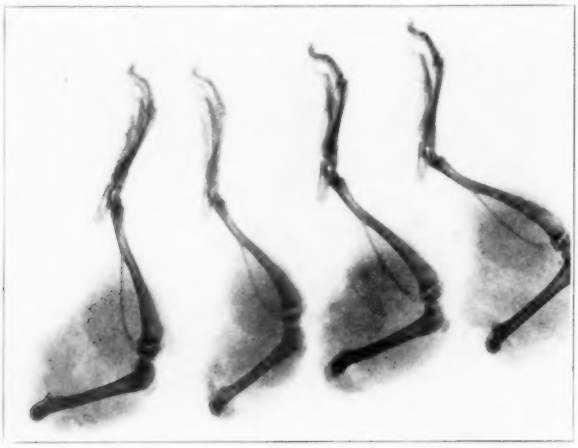

Fig. 8.—Roentgenogram of animals of Vitaglass group.

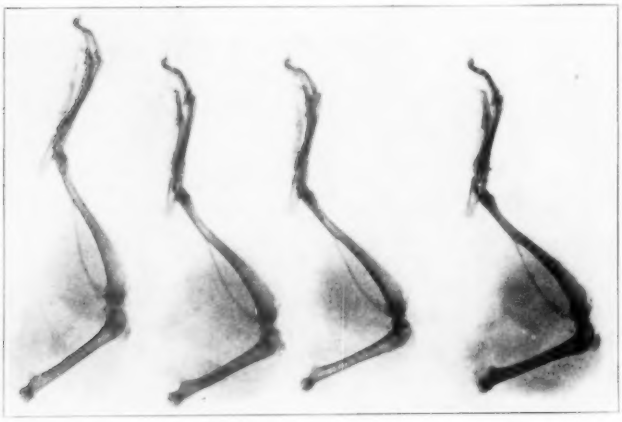

Fig. 9.—Roentgenogram of animals of direct irradiation group.

showed the deformities of the epiphyses of the long bones, which are generally accepted as rachitic, and again were classified in grade 4.

The third group consisted similarly of animals on the standard diet, but irradiated through Vitaglass. The histologic preparations from the femur and tibia showed definite changes of a rachitic nature. Some of the animals were placed originally in grade 2, while others with more

marked symptoms were classified, from the first, in grade 3. The average picture was, perhaps, intermediate between the stage of early recognized changes and that of more advanced changes.

The fourth group was composed of animals which received their irradiation through Corning glass. All the animals in this group were given histologic examinations. Two of them were put in grade 2; the others were considered essentially free from rickets and were graded in the first classification.

The fifth group consisted of animals which received direct irradiation without the intervention of glass. These animals showed practically the same results as those in the Corning glass group, and, for all practical purposes, would be considered free from rickets. One or two of them showed slight irregularities in the epiphyseal junction, which were not, however, more marked than those found in animals on a perfectly normal diet.

Ash Content of Femur and Tibia.—The flesh was carefully removed from the tibia of the left leg. The bones were dried in an electric oven

TABLE 2.—*Ash Content of Femur and Tibia*

	Control Group, per Cent	Window Group, per Cent	Corning Group, per Cent	Vitaglass Group, per Cent	Direct Irradiation Group, per Cent
Femur	31.8	35.6	55.7	49.8	54.0
Tibia	39.7	37.8	56.0	51.4	55.1
Combined	35.7	36.7	55.8	50.6	54.6

for forty-eight hours at 96 C., then extracted for sixteen hours with alcohol; subsequently extracted for twenty-four hours with ether, and dried, at 100 C. for one hour, in an Underwriter's experiment apparatus, to approximately constant weight. The bones were heated over a fire flame until the organic matter had practically disappeared. Then they were incinerated in an electric muffle furnace and weighed to constant weight. The ash content of the femur and tibia in the different groups of animals is reported in table 2.

It will be noted (table 2) that the ash content of the femur was less for the animals in the control group than for those in the window group, whereas the ash content of the tibia was larger for those of the control group than for those of the window group. The relation between the ash content for the animals in the Corning glass, Vitaglass and direct irradiation groups was the same for both femur and tibia. The ash content of the femur and tibia combined was practically the same in the animals of the control group and those of the window group; this was also true of the animals in the Corning group and of those in the direct irradiation group; the animals of the Vitaglass group, however, had somewhat lower ash content. In general, the ash

content of the femur and tibia showed that the window glass used in this test excluded practically all the ultraviolet light, that the Vitaglass transmitted a considerable portion of the ultraviolet light and that the Corning glass transmitted a still greater amount of ultraviolet light.

SUMMARY

It appears from the growth curves, the calcium and phosphorus content of the blood serum, the roentgenograms, the pathologic studies and the ash content of the bones that practically as much ultraviolet light passes through Corning glass as is obtained by direct irradiation. Vitaglass, on the other hand, permits the passage of only a certain fraction of the necessary ultraviolet rays. Ordinary window glass may be considered virtually useless in this respect, owing to the fact that the animals irradiated under this type of glass showed practically as marked a degree of rickets as those which did not receive any irradiation.

THE TREATMENT OF RICKETS WITH IRRADIATED ERGOSTEROL *

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It is well known that commercial cholesterol, when irradiated with ultraviolet light, can be used to cure patients with rickets. In 1925, Windhaus,[1] Hess, and Rosenheim and Webster [2] showed that when commercial cholesterol is further purified by using animal charcoal, by oxidation, by distilling in a high vacuum or by using dibromides and then is irradiated, it is not effective in curing animals with rickets. Such attempts at separating pure cholesterol also change the absorption spectrum of the cholesterol. Windhaus, who had worked with sterols for many years, noted that ergosterol resembles cholesterol in its physical and chemical properties, but possesses three unsaturated carbon atoms. Ergosterol could easily be taken up, therefore, by oxidation, halogens, and the like; so Windhaus suspected that ergosterol is the substance responsible for the antirachitic value of irradiated commercial cholesterol.

Windhaus [3] next mixed ergosterol with purified cholesterol and obtained the typical absorption band of commercial cholesterol. When it was exposed to ultraviolet light, the same changes in the spectrum appeared as occur in irradiated cholesterol.

It was estimated that there is only from $\frac{1}{20}$ to $\frac{1}{40}$ per cent of ergosterol contaminating commercial cholesterol. Ergosterol, $C_{27}H_{43}O$, is a sterol, and can be obtained from a wide range of lower plants, especially from fats extracted from certain yeasts, from certain fungi and from ergot. It was suggested by Rosenheim and Webster that cod liver oil may owe its antirachitic value to the natural irradiation by sunlight of ergosterol contained in algae which are eaten by the fish.

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* Submitted for publication, Sept. 17, 1928.

* From the Department of Pediatrics, Cornell University Medical College and the New York Nursery and Child's Hospital.

1. Windhaus: Nachrichten von derkönigl. Gesellschaft der Wissenschaften zu Göttingen Mathem. physik. Klin., 1926; Klin. Wchnschr. **6**:666 (April) 1927.

2. Rosenheim, O., and Webster, T. A.: The Nature of the Parent Substance of Vitamin D, Lancet **1**:306 (Feb. 5) 1927. Rosenheim, O., and Webster, T. A.: J. Soc. Chem. Indust. **45**:932, 1926.

3. Windhaus (footnote 1, second reference).

Animal experiments with irradiated ergosterol were next made, and it was found by Windhaus,[3] Hess,[4] Rosenheim and Webster,[5] and others that only $\frac{1}{1000}$ mg. of the irradiated ergosterol per day is sufficient to prevent rickets in rats kept on a rickets producing diet, whereas 1 mg. of irradiated cholesterol is required. Sometimes the dose of irradiated ergosterol required was extremely minute, $\frac{1}{100,000}$ mg. per gram of rat, according to Hottinger? He also succeeded in curing dogs and rats of rickets by irradiated ergosterol. Just how irradiation with ultraviolet light changes the ergosterol is not yet understood. Its absorption spectrum is 2,000 times as intense as that of irradiated commercial cholesterol, and the tests on rats seem to indicate a relation between this intensity and the dose necessary to cure rickets.

The next step in the experiments with irradiated ergosterol was to try it on infants suffering from rickets. During 1927 and 1928, many reports of its successful use in the treatment for rickets and also for tetany appeared in the European medical literature. Although most of the experiments have been made in a small number of cases, several series are of substantial proportions (twenty-five cases reported by Gyorgy,[6] sixteen cases by Hottinger,[7] and eighteen by Falkenheim[8]). No untoward result or failure has been reported. In many instances in which tetany accompanied the rickets, the tetany disappeared without other treatment than the administration of irradiated ergosterol. It has been reported that relief was obtained in some cases of osteomalacia by the use of irradiated ergosterol. With occasional exceptions, it has proved an efficient preventive against rickets, according to several observers.

In general, it was found that in rachitic infants treated with irradiated ergosterol, the blood serum phosphorus and calcium return to normal concentrations within from two to four weeks after treatment is begun; that x-ray evidence of beginning of healing in the bones may usually be demonstrated within twenty-one days, and that complete healing takes about six or eight weeks.

The absence of any reports in the American literature[9] on the clinical use of irradiated ergosterol, plus the great advantage it seems to

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4. Hess, A. F.: Antirachitic Activity of Irradiated Cholesterol, Ergosterol and Allied Substances, J. A. M. A. **89**:337 (July 30) 1927.

5. Rosenheim and Webster (footnote 2, second reference).

6. Gyorgy, P.: Klin. Wchnschr. **6**:580 (March 26) 1927.

7. Hottinger: Researches with Irradiated Ergosterol, Ztschr. f. Kinderh. **44**:283, 1927.

8. Beumer and Falkenheim: Klin. Wchnschr. **6**:798 (April) 1927.

9. Since this work was begun, a preliminary report of nine cases of craniotabes in which the patients were treated successfully with irradiated ergosterol has appeared in Karelitz: Proc. Soc. Exper. Biol. & Med. **25**:576 (April) 1928.

possess as an antirachitic, has led us to undertake the present study of twenty-four rachitic infants, varying in age from 9 weeks to 2 years. Twenty-two of these infants were treated with irradiated ergosterol, and two with cod liver oil. The condition varied from mild rickets with craniotabes as the only clinical manifestation to severe acute rickets with sudden loss of ability to walk. Two of the infants treated with irradiated ergosterol also had tetany. Several had refused cod liver oil, even the flavored variety, and in three of them slow progress had been made with cod liver oil. A commercial preparation of the irradiated ergosterol containing 10 mg. in 1 cc. of sesame oil was used. This was kindly furnished for experimental use by the Winthrop Chemical Company. The dose used was 3 mg. of the irradiated ergosterol daily, given as four drops of commercial preparation twice a day, either in the formula or in a teaspoonful of warm milk. To be more exact, the dose varied from 3.2 to 3.6 mg. per day, as the irradiated ergosterol used contains from 22 to 26 drops per cubic centimeter, varying according to the dropper used. This dose was used because although a few observers have reported good results with only 1 or 2 mg. a day, Gyorgy found several rachitic infants who required 3 mg. daily for cures. The preparation was well tolerated by all our patients, even by the two who had pneumonia. There were no instances of vomiting or diarrhea.

To eliminate the favorable influence of the summer season on the healing of rickets, the experiments were conducted from January to May, with the exception of two cases studied in June.

In table 1, a general summary of the results is recorded. The first five cases were studied on the wards of the New York Nursery and Child's Hospital. Exposure to sunlight or any antirachitic measure other than the irradiated ergosterol was not permitted. Blood serum calcium and phosphorus were determined in these patients at weekly intervals. The other seventeen rachitic infants receiving irradiated ergosterol were studied at the clinic almost weekly. Roentgenograms of the extremities and careful clinical notes were made at each visit. These infants did not receive special sunlight therapy but were not enjoined from going outdoors. It is probable that some of them had their faces exposed to the sunlight for several hours daily on sunny days. However, there is little ultraviolet radiation, within antirachitic limits, in New York during the winter, and much rain. Judging from the control infants, the sunlight did not play a sufficiently important rôle in the prevention or cure of rickets during the past winter to interfere greatly with the value of the experiments.

Several terms used in table 1 need definition. Evidence of beginning healing is considered present in the roentgenogram if a definite increase in calcium deposition can be demonstrated at the metaphysis in the rachitic zone. By "healed rickets" in the roentgenogram is meant the

TABLE 1.—*Summary of Results of Treatment with Irradiated Ergosterol*

Patient	Age	Name	X-Ray Healing Begun	Healed According to the X-Ray	Healed Clinically	Gain in Weight	Craniotabes Healed	Treatment	Comment
1	7 mo.	A. Y.	7 days	2 weeks	4 weeks	Good	12 days	Solution of irradiated ergosterol, 4 drops twice a day	Blood normal in 12 days
2	22 mo.	E. W.	21 days	8 weeks	8 weeks	Good	None	Solution of irradiated ergosterol, 4 drops twice a day	Blood normal in 24 days; tetany healed in 8 days
3	12 mo.	J. S.	7 days	24 days	1 mo.	Poor	14 days	Solution of irradiated ergerostol, 4 drops twice a day	Bronchopneumonia healed roentgenographically; blood normal in 14 days; tetany healed in 8 days
4	.....	J. R.	14 days	4 weeks	1 mo.	Good	None	Solution of irradiated ergosterol, 4 drops twice a day also egg yolk	Blood normal in 14 days; tetany healed in 8 days
5	.....	P. H.	13 days	21 days	1 mo.	Poor	None	Solution of irradiated ergosterol, 4 drops twice a day	Blood normal in 21 days
6	20 mo.	R. R.	14 days	6 weeks	6 weeks	Good	None	Solution of irradiated ergosterol, 4 drops twice a day	Active rickets
7	7 mo.	A. U.	37 days	8 weeks	8 weeks	Good	37 days	Solution of irradiated ergosterol, 4 drops twice a day	
8	6 mo.	M. E.	14 days	2 weeks	3 weeks	Good	21 days	Solution of irradiated ergosterol, 4 drops twice a day	Received cod liver oil for 3 weeks without any effect
9	4 mo.	T. S.	X-ray normal bones		24 days	Good	14 days	Solution of irradiated ergosterol, 4 drops twice a day	Had refused cod liver oil
10	3 mo.	F. K.	30 days	6 weeks	4 weeks	Good	None	Solution of irradiated ergosterol, 4 drops twice a day	
11	4 mo.	J. G.	23 days	8 weeks	9 weeks	Good	35 days	Solution of irradiated ergosterol, 4 drops twice a day	
12	3 mo.	A. W.	.....	5 weeks	5 weeks	Good	35 days	Solution of irradiated ergosterol, 4 drops twice a day	Also in sun
13	3 mo.	M. G.	8 weeks	8 weeks	12 weeks	Good	12 weeks	Solution of irradiated ergosterol, 4 drops twice a day	No irradiated ergosterol for 1 month
14	9 weeks	L. W.	27 days	7 weeks	7 weeks	Good	7 weeks	Solution of irradiated ergosterol, 4 drops twice a day	
15	15 weeks	A. N.	.....	.....	3 weeks	Good	None	Solution of irradiated ergosterol, 4 drops twice a day	Pylorospasm; refused cod liver oil
16	4 mo.	J. N.	.....	1 mo.	5 weeks	Good	5 weeks	Solution of irradiated ergosterol, 4 drops twice a day	Developed craniotabes despite cod liver oil
17	8½ mo.	H. P.	Rickets not active by x-ray		7 weeks	Good	None	Solution of irradiated ergosterol, 4 drops twice a day	Refused cod liver oil
18	2 years	M. C.	21 days	8 weeks	8 weeks	Good	None	Solution of irradiated ergosterol, 4 drops twice a day	
19	17 mo.	J. C.	26 days	7 weeks	6 weeks	Good	None	Cod liver oil.....	Used as control; compare with case 18
20	4½ mo.	C. L.	.....	.....	8½ weeks	Good	61 days	Cod liver oil.....	Used as control
21	13 mo.	C. L.	.....	.....	4 weeks	Good	None	Solution of irradiated ergosterol, 4 drops twice a day	
22	11 weeks	G. V. W.	Normal bones on x-ray		.....	.....	5 weeks	Solution of irradiated ergosterol, 4 drops twice a day	Cod liver oil for 2 mos.; did not affect craniotabes
23	3 mo.	D. P.	.....	4 weeks	4 weeks	Poor	4 weeks	Solution of irradiated ergosterol, 4 drops twice a day	Treated in June
24	11 mo.	R. M.	.....	.....	4 weeks	Fair	None	Solution of irradiated ergosterol, 4 drops twice a day	Bronchopneumonia

presence of a strong thick line of calcium at the border of the diaphysis, and almost complete trabeculation of the former rachitic zone. The foregoing criterion was adopted because it often takes one or two years after treatment for rachitic bone to appear normal in the roentgenogram. The term, "healed clinically," indicates that all lesions of the bone, such as craniotabes and beading of the ribs, are healed, that there is no sweating about the head, that the infant is lively and gaining weight, and that its development, so far as we can judge, is proceeding normally. It does not mean that the anemia has disappeared and that the flabby muscula-

Figure 1

Figure 2

Fig. 1 (case 2).—Roentgenographic appearance of active rickets in E. W. on Jan. 30, 1928.

Fig. 2 (case 2).—Roentgenographic appearance on Feb. 20, 1928, three weeks after irradiated ergosterol was begun, showing beginning of healing.

ture has been corrected. In cases in which the bowing of the tibia or the beading of the ribs had been severe, we made exceptions and considered the rickets as healed, even though some bowing or beading remained, provided the roentgenograms showed healed rickets and the other manifestations of rickets had disappeared.

With these restrictions in mind, we shall discuss the results.

COMMENT

All of the twenty-two infants receiving irradiated ergosterol in the form of a commercial preparation took it well and had no untoward symptoms. This is significant, for patients 9, 15 and 17 had previously refused or vomited cod liver oil, and patients 3 and 24 had severe bronchopneumonia at the time they received the irradiated ergosterol. All the patients except three showed good gains in weight. Hemoglobin tests were done in only a few instances, and the anemia did not seem to be relieved by the ergosterol.

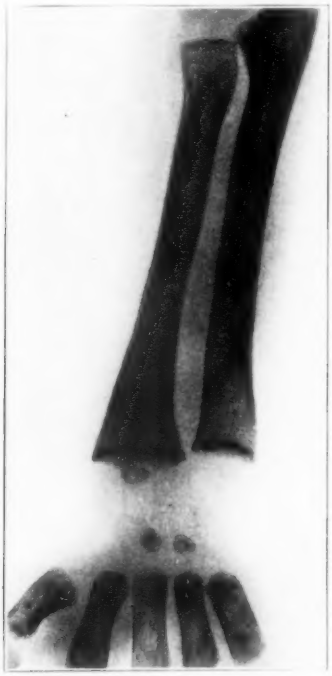

Fig. 3 (case 2).—Roentgenographic appearance on March 28, 1928, two months after treatment was begun, showing healing rickets.

Only 4 drops twice daily of the solution of irradiated ergosterol in sesame oil was sufficient to effect a cure of the rickets in each of the twenty-two patients. In the first case, the commercial preparation used had been obtained six months previously from the Heidelberg University Children's Hospital. It had been kept on ice for only one month; yet it proved potent as an antirachitic agent.

In general our results indicate that irradiated ergosterol is as effective as cod liver oil, and in several instances it proved effective more rapidly. These observations are in accord with those of other observers.

The blood serum phosphorus and calcium returned to normal levels within two or three weeks after treatment with irradiated ergosterol had been started. Most of the figures given for cod liver oil in treatment for rickets are similar.

The average time needed to obtain evidence of beginning healing in bone was twenty-three days in twelve of our cases. An average of three weeks is required for cod liver oil to produce this stage of healing, according to Chick's [10] studies in Vienna. However, in two of our patients (cases 1 and 5), therapy with irradiated ergosterol for only one week produced changes of beginning healing shown by the x-rays. Cod liver oil is reported as being capable of producing such rapid healing.

Fig. 4 (case 6).—Roentgenographic appearance in R. R. on April 13, 1928. The patient was unable to walk. He had active acute rickets. The administration of irradiated ergosterol was begun one week later.

On the other hand, in case 13, the patient was not well until after eight weeks, which is longer than the usual time required for cod liver oil to produce a cure. With the mercury quartz vapor lamp, healing in persons with rickets generally begins in from thirteen to twenty-four days (Chick).[10]

The time necessary for the complete clinical healing of rickets in our series in which irradiated ergosterol was used, was about the same as that generally required when cod liver oil is employed, averaging five and one-half weeks in twenty-one cases. In our two control cases, 19 and

10. Chick: Report on Rickets, Great Britain Medical Council Research, 1923, report 77.

20, in which cod liver oil was used, the rickets was healed in seven and one-fourth weeks. This is within the range of time which may be necessary when irradiated ergosterol is used, but is more than the average time required by the group of patients given irradiated ergosterol.

The two patients with tetany (cases 2 and 4) were cured of their tetany within eight days by the administration of irradiated ergosterol; no other antitetanic treatment was given. The electrical reactions became normal, and the serum calcium and phosphorus were increased to normal.

Figure 5

Figure 6

Fig. 5 (case 6).—Roentgenographic appearance on April 7, 1928, showing beginning healing. A new layer of bone was visible in the former rachitic zone two weeks after the administration of irradiated ergosterol was begun. The patient was able to walk again.

Fig. 6 (case 6).—Roentgenographic appearance on June 8, 1928, showing marked healing, almost complete trabeculation and a thick line of calcium formation.

Twelve patients in this series had craniotabes; an average of thirty-one days was required for complete healing, the time varying from twelve days to more than eight weeks. The infant in case 20, who had received cod liver oil and was used as a control, required sixty days of treatment before the craniotabes was completely healed. This is longer than the time usually necessary when cod liver oil is used. In some of the

cases, the craniotabes was apparently resistant to treatment with cod liver oil, as in case 22, in which cod liver oil was used for two months without the slightest effect on the craniotabes. This infant was then given the commercial preparation of irradiated ergosterol, and although five weeks was required for the complete healing of the craniotabes, there was marked improvement within two weeks. In case 8, the patient had also received one teaspoonful of cod liver oil three times daily for weeks without effect on the craniotabes. After the administration of irradiated ergosterol was begun, the skull healed within five weeks.

Cases 1, 2, 3, 6, 18 and 19 in table 1 are given in greater detail in table 2. Case 3 (J. S.) is of especial interest. The roentgenograms showed definite signs of healing within one week, despite a serum phosphorus of 2.6 mg. and a calcium content of 7.9 mg. per hundred cubic centimeters, which make a product of 20.5 mg., much less than the usual product necessary for beginning healing to show by x-ray examination (30 mg.) (Howland and Kramer). This patient's low blood phosphorus and calcium persisted even after twenty-four days. Perhaps the severe bronchopneumonia from which he suffered prevented an early return of the serum phosphorus and calcium to normal concentrations. It has been noticed that more ultraviolet irradiation is needed to heal rickets in patients ill with severe infections than in others.

R. R., the patient in case 6, with acute rickets, also responded rapidly to the treatment with irradiated ergosterol and was able to walk again within three weeks after treatment was begun.

The dosage used in our experiments was 3 mg. a day. It is possible that if we had increased the dose, a more rapid cure would have been effected, but at the present early stage in the clinical research with irradiated ergosterol we wished to proceed cautiously. Although untoward results have not been reported in infants, Kreitmar and Moll [11] found that immense doses (2,000 times the therapeutic dose) cause death when given to rats. Calcium depositions in the walls of the arteries, in the muscles and in the spleen were present at autopsy. Vollmer [12] gave rachitic infants as much as 25 mg. a day for six days in succession, hoping to effect a rapid cure or to produce a lasting effect, but he found that unless the irradiated ergosterol was continued, the rachitic process would go on. He did not note any untoward effect from these doses, however.

There can be no question that irradiated ergosterol is a powerful agent, and Hess [13] advises caution. He cited two or three instances in

11. Kreitmar and Moll: München. med. Wchnschr. **75**:673 (April 13) 1928.
12. Vollmer: Ztschr. f. Kinderh. **45**:265 (Feb.) 1928.
13. Hess, A.: Report read at meeting of American Pediatric Society, May 1, 1928.

TABLE 2.—*Detailed Data on Six Cases from Table 1*

Patient	Date	Clinical Manifestations	X-Ray Manifestations	Calcium-Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Treatment	Progress; Comment
E. W. (case 2) 22 months	1/30	Marked beading; bowing; enlarged epiphyses	Very active rickets	....	...	.....	Latent tetany cured
	2/ 2	Positive Chvostek; electrical reactions; tetany (border)	.....	7.5	2.7	Solution of irradiated ergosterol, 4 drops twice daily, begun 2/4	Normal blood chemistry in 20 days and healing of bone begun in 20 days, complete in 7 weeks; tetany
	2/10	No Chvostek	Same.....	9.1	2.4	.....	Calcium improving
	2/17	.....	.....	8.7	4.2		
	2/21	.....	Healing rickets....	....	...	.....	Healing of bone begun
	2/24	.....	Marked healing....	10.0	5.1	.....	Normal blood; gained 2½ pounds from 2/1/28 to 3/29/28
	3/28	Bowing; beading of ribs still present; enlarged wrists	Healed rickets				
M. C. (case 18) 2 years	3/26	Moderate beading; marked bowing of legs; increased wrists; open anterior fontanel, one fingerbreadth	Marked active rickets	....	...	Solution of irradiated ergosterol, 4 drops twice daily	X-ray showed healing which began in 3 weeks, complete in 8 weeks; improvement in bowing marked in 8 weeks
	4/16	Anterior fontanel closing; no beading	Beginning healing	....	...	.....	Improving; compare with cod liver oil control, J. C.
	4/23	No beading; same.....	Healing				
	5/ 7	Less enlarged wrists.....	Marked healing				
	5/21	Increase in wrists.....	Healed rickets.....	....	...	.....	Bowing much less
	6/ 4	Mother noticed improvement in bowing; much less	Healed rickets.....	....	...	.....	Rickets healed
J. C. (case 19) 17 months	4/16	Moderate bowing of legs, moderate increase in wrists; marked beading	Very active rickets	....	...	Cod liver oil,1 drachm, three times daily	Evidence of x-ray healing marked in 5 weeks and complete in 7 weeks
	4/23	No improvement					
	5/ 7	Beading moderate; bowing same	.....	....	...	.....	Improving
	5/21	Bowing less; increase in wrists almost gone	Marked healing rickets	....	...	.....	Compare with foregoing patient on irradiated ergosterol
	5/28	Bowing same	Healing rickets				
	6/ 4	Bowing less	Healed rickets; not as advanced as in foregoing case	....	...	.....	Improved; healed rickets

A. Y. (case 1) 7 months	1/10	Considerable craniotabes; beading; flaring ribs; dull	.....	5.6	2.1	None first week	
	1/18	Same as on admission	Active rickets.....	9.1	2.3	Solution of irradiated ergosterol started, 4 drops twice daily	Solution of irradiated ergosterol used was 6 months old; had been kept on ice only 1 month
	1/30	Patient more active; no craniotabes; marked beading	Healing rickets....	9.3	4.1	.....	Craniotabes healed in 12 days; blood chemistry normal in 2 weeks; x-ray healing in 2 weeks; beading of ribs only manifestation of rickets left in 1 month; gained 1 pound 1 ounce from 1/18 to 2/2
	2/ 2	Gaining weight; lively; no craniotabes; marked beading	Healed rickets	10.0	6.0		
R. R. (case 6) 20 months	4/13	Suddenly unable to walk; acute rickets; bowing tibia; pot belly	Marked, active rickets	....	...	Solution of irradiated ergosterol, 7 drops twice daily	Unable to walk for 2 weeks; had been indoors from August 27 to January 28; normal development; no clinical evidence of rickets other than acute inability to walk, bowing of legs, slight pot belly; x-ray showed remarkably active process; healing of bone began in 3 weeks, complete in 7 weeks
	5/ 7	Stronger on legs.....	Marked healing				
	5/14	Improved; walks again..	Healing marked	....	...	From 5/31, cod liver oil, 1 drachm, three times daily	
	6/ 8	.....	Healed rickets				
J. S. (case 3) 12 months	4/30	Marked craniotabes; rosary; enlarged wrists; also bronchopneumonia; hemoglobin, 47%	Severe rickets; fractured right fibula	8.7	1.8	Solution of irradiated ergosterol, 4 drops twice daily	Despite severe bronchopneumonia, rickets healing; craniotabes gone in 2 weeks; x-ray of extremities showed healing with a low blood serum phosphorus and calcium product of 20.5 mg.
	5/ 7	.....	Slight healing.....	7.8	2.6		
	5/18	No craniotabes	More bone healing	7.9	2.6	.....	Craniotabes gone; was very ill; in oxygen tent; transfusion
	5/24	Beading much less marked	Marked healing not yet complete	8.3	3.3	.....	Beading much less marked

which he noted that the blood serum phosphorus was raised to 12 mg. per hundred cubic centimeters by irradiated ergosterol, and several other observers have noted a high phosphorus value of the blood following the administration of irradiated ergosterol. In this connection, we would like to cite a case which came under our observation at the hospital.

An infant was admitted suffering from tetany; she had a blood serum phosphorus of 12.9 mg. and a calcium of 4.4 mg. per hundred cubic centimeters. She was not given irradiated ergosterol, and despite the administration of calcium chloride by mouth she died the following day. Her blood serum phosphorus and

Figure 7

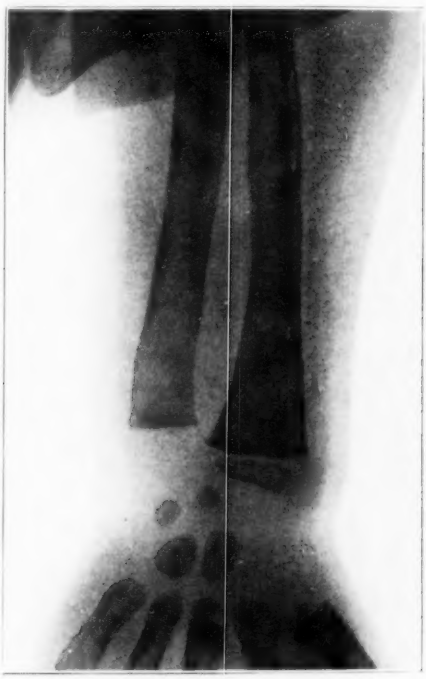

Figure 8

Fig. 7 (case 6).—Roentgenographic appearance on June 25, 1928, showing healed rickets.

Fig. 8 (case 6).—Roentgenographic appearance on Aug. 20, 1928, showing bones four months after treatment was begun. Except for some periosteal thickening the bones appear normal.

calcium, determined just before death, were 13.7 and 3.3 mg. per hundred cubic centimeters, respectively.

The question arises, if such patients are given irradiated ergosterol, might not their blood phosphorus be still further increased to a dangerous level? Facilities for blood chemical determinations are rarely available outside of a hospital, and how is one to know whether or not

this rare type of high phosphorus tetany is present, or how is one to predict how high the irradiated ergosterol will raise the phosphorus content with perhaps a corresponding decrease in calcium? Until the use of irradiated ergosterol in the treatment for tetany has been more carefully studied, it would seem advisable to rely on proved agents such as calcium and ammonium chloride in private practice.

PREVENTION OF RICKETS

Nearly all reports [14] on the use of irradiated ergosterol as a preventive of rickets are favorable. Hottinger reported one instance in which slight rickets developed despite treatment with irradiated ergosterol but yielded readily to larger doses. Our own experience is limited to eight cases, in which 3 mg. a day was given, beginning when the patient was 2 weeks of age. One of these patients, a premature infant, developed slight craniotabes at 3 months of age, despite the use of a commercial preparation of irradiated ergosterol. It disappeared within four weeks, the dose of irradiated ergosterol remaining unchanged, 3 mg. a day.

SUMMARY

1. Twenty-four infants with rickets, varying from mild to severe forms, were successfully treated with irradiated ergosterol.

2. Two infants with tetany were cured by irradiated ergosterol.

3. The irradiated ergosterol, in the form of a commercial preparation, was well taken and well tolerated. Two of the patients had severe bronchopneumonia, and several had previously refused or vomited cod liver oil.

4. The commercial preparation used retained its potency for at least six months in one instance.

5. Reports of other authors who used irradiated ergosterol are confirmed. It was found that irradiated ergosterol requires about three weeks to cause serum blood phosphorus and calcium concentration to return to normal, about the same time for x-ray signs of healing of the bones to appear, and about six weeks for complete healing. These averages compare favorably with those obtained with cod liver oil, quartz light and egg.

6. Craniotabes was healed within an average of one month in our series of twelve patients. In individual cases a period of from twelve days to eight weeks was required.

14. Gyorgy (footnote 6). Hottinger (footnote 7).

7. Healing of the rachitic bone took place in one patient with bronchopneumonia, despite a low serum phosphorus and calcium product of 20.5 mg. per hundred cubic centimeters.

8. Caution may be necessary in using irradiated ergosterol in patients with tetany who show a high blood phosphorus content.

9. Irradiated ergosterol is not a perfect preventive for rickets. Craniotabes developed in one patient receiving prophylactic doses of irradiated ergosterol. This healed promptly when the ergosterol was continued in unchanged amounts.

INTRAPERITONEAL BLOOD TRANSFUSION

REPORT OF TWO HUNDRED AND THIRTY-SEVEN TRANSFUSIONS ON ONE HUNDRED AND SEVENTEEN PATIENTS IN PRIVATE PRACTICE *

W. C. C. COLE, M.D.
AND
J. C. MONTGOMERY, M.D.
DETROIT

The therapeutic value of blood transfusion in a wide variety of clinical conditions is constantly being more appreciated. In the treatment of anemia, in septicemia and toxemia, in certain nutritional states and in many types of both acute and chronic infection, the value of blood from a suitable donor has been definitely established.

As these conditions affect infants and young children, the benefits of blood transfusion seem to be especially marked.

Unfortunately, the technical difficulties involved in the intravenous administration of blood to infants are so great as practically to limit its frequent use to well equipped hospitals with specially trained staffs, and are such as to preclude its use by the average practitioner. Even under the best of circumstances in hospitals and with the most experienced operators, it is not at all unusual to encounter difficulty in entering a child's vein, especially when it is desirable to do so repeatedly. Consequently, this valuable therapeutic measure is frequently either entirely neglected or postponed until the terminal stages of an illness, when its usefulness is considerably lessened. Certainly only a small proportion of those children in whom transfusion is definitely indicated receive its benefits, due largely to the technical barriers presented.

As a means of overcoming these difficulties, the intraperitoneal route has been introduced. While a good deal of experimental work had previously been done on absorption from the peritoneal cavity, its first important clinical application was made in 1918 by Blackfan and Maxcy,[1] when they reported their experience with the administration of saline solution in this way. The value of that procedure is now too well known to require comment. Then in 1923, Siperstein and Sansby [2] reported their experiments and clinical results with the injection of citrated blood

* Submitted for publication, Sept. 11, 1928.

* From the Children's Clinic of Detroit.

1. Blackfan, K. D., and Maxcy, K. F.: Intraperitoneal Injection of Saline Solution, Am. J. Dis. Child. **15**:19 (Jan.) 1918.

2. Siperstein, N. M., and Sansby, J. M.: Intraperitoneal Transfusion with Citrated Blood, Am. J. Dis. Child. **25**:107 (Feb.) 1923.

into the peritoneum. Their work showed that blood injected in that way is rapidly and completely taken into the blood stream without change and constitutes a true transfusion. Additional evidence that absorption takes place directly into the blood stream is furnished by many investigations. Dandy and Rowntree [3] observed that phenolsulphonphthalein injected into the peritoneum appears in the blood within two minutes, but not in the thoracic duct for more than twenty minutes. It has been shown repeatedly that nucleated bird's cells appear in quantity in the blood stream of rabbits before they can be demonstrated in the lymphatic vessels. So it seems fairly definitely established that absorption takes place directly into the blood without apparent change.

Since the reports of Siperstein and Sansby, several others have been made, especially those of Opitz and Metis,[4] McKhann [5] and Ruh and McClelland,[6] all of which tend to substantiate the points mentioned.

Recently the method has been used to a moderate extent, but clinical reports of any considerable number of cases have been lacking. There seems to be a feeling on the part of many physicians that the method is unsound surgically, that there is danger of injury to important abdominal organs, or that peritonitis or the formation of clots may result. In short, there appears to be a mild reluctance to employ it on any extensive scale.

Accordingly, we thought it opportune to present our results in a considerable series of cases with the view of establishing confidence in the method and thus extending the benefits of blood transfusion to that large group of patients in whom it is so often indicated but omitted.

The method of carrying out these transfusions is extremely simple, and they can be done in the office or home without the aid of trained assistants. Several times one of us has performed such a transfusion in the home with only the help of the parents.

It is possible that blood grouping is not necessary in this type of transfusion, but we have not felt justified in omitting it, especially when it is so easily applied. On two or three occasions moderate reactions have been noted which apparently were due to an incompatible donor. We have always used as donors either members of the same group or of group 4, but we have not gone to the trouble of cross-agglutination which is always done in intravenous transfusions.

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3. Dandy, Walter E., and Rowntree, L. A.: Peritoneal and Pleural Absorption with Reference to Postural Treatment, Ann. Surg. **59**:587, 1914.

4. Opitz, H., and Metis, F.: Intraperitoneal Transfusion of Blood with Report on Experiments on Animals and Persons, Jahrb. f. Kinderh. **107**:269 (Dec.) 1924.

5. McKhann, C. F.: Intraperitoneal Transfusion of Citrated Blood in Acute Intestinal Intoxications of Infancy, Boston M. & S. J. **195**:1241 (Dec. 30) 1926.

6. Ruh, H. O., and McClelland, J. E.: Intraperitoneal Transfusions in Infants, Ohio State M. J. **19**:780 (Nov.) 1923.

METHOD

The blood is collected from the donor in a large syringe of suitable size to accommodate the desired amount of blood. The appropriate amount of 2.5 per cent sodium citrate solution is first taken into the syringe, and the blood is quickly collected and mixed with the citrate. The needle is then detached and a long rubber tube applied, in the other end of which is a glass adapter with the peritoneal needle. The piston is then removed from the syringe and the equipment used as a gravity apparatus. The needle is inserted in the mid-line below the umbilicus and above the bladder. There is little possibility of penetrating the bladder or bowel, but of

Figure 1

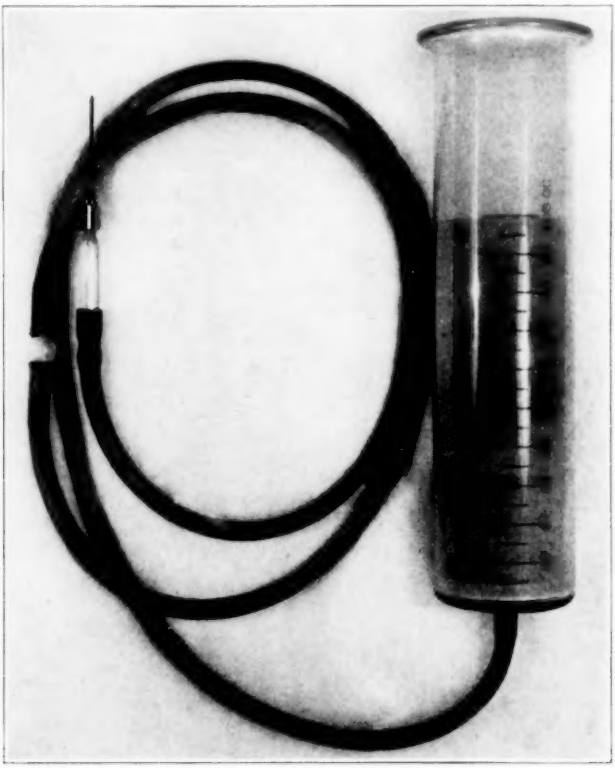

Figure 2

Fig. 1.—Syringe and needle containing citrate solution in which donor's blood is collected.

Fig. 2.—Syringe with piston removed and tubing attached, ready to use as gravity apparatus for the intraperitoneal injection.

course the precaution should be taken to have them both reasonably empty. It is virtually impossible to push a needle into either of these organs unless it is tense and distended.

It is important that the citrate solution should not be more than a week old and that it should not be buffered with dextrose as commonly prepared. Old citrate

solutions frequently change reaction and become irritating, and dextrose acts as a decided peritoneal irritant. Moderate distention and abdominal distress, which were occasionally observed in some of our early cases, were traceable to this cause.

The blood may be permitted to run as fast as it will. Seldom more than five minutes is required to give 4 ounces (118 cc.).

It is best to use a large bore, short bevel needle for entering the peritoneum.

The usual amount of blood given in this way has been about 4 ounces to children under 3 years of age. The therapeutic effect is as good or better from repeated small transfusions than from a single large one.

TABLE 1.—*Data on Intraperitoneal Transfusions*

	Number of Cases	Number of Transfusions
I. Primary anemia		
1. Lymphatic leukemia	2	2
2. Myeloid leukemia	1	2
3. Agranulocytic angina	1	7
4. Unclassified	1	5
	5	16
II. Secondary anemia		
1. Of nutritional origin	27	62
2. Associated with acute infection	50	100
	77	162
III. New-born and premature infants	8	15
IV. Septicemia and toxemia	27	44
Totals	117	237

TABLE 2.—*Infants with Primary Anemia*

No.	Age	Date of Transfusion	Diagnosis	Reaction		Result
1299	4 yrs.	12/29/27	Lymphatic leukemia	120	Slight	Died
9246	18 mos.	4/21/27	Lymphatic leukemia	150	None	Died
9231	10 mos.	4/18/27	Myeloid leukemia	120	Severe	
				120	Severe	Died
9076	2 yrs.	2/25/27	Unclassified	120	None	
		3/ 1/27		75	None	
		3/14/27		120	None	
		3/30/27		120	None	
		4/19/27		100	Severe	
		4/23/27		120	None	
		4/30/27		150	Moderate	Lost from observation
8831	2 yrs.	5/17/27	Agranulocytic angina	60	None	
		5/18/27		120	None	
		5/21/27		120	None	
		5/25/27		120	None	
		6/ 8/27		120	None	Died; at postmortem, small clots in abdomen

During the past three years, 237 such transfusions have been done on 117 patients in private practice. Originally, the intraperitoneal method was used only as a substitute when the intravenous route was unusually difficult. However, the result obtained with these occasional cases compared so favorably in every way with the others that the method has been used with increasing frequency. During the past year many transfusions have been made in patients in whom the intravenous route would not have been difficult, because of the facility of performance.

Table 1 shows the type of cases in which these transfusions were done. It will be noted that by far the largest number was done in the treatment for secondary anemia, either of nutritional origin or as the result of acute infection. In nearly every case of secondary anemia the hemoglobin was below 50 per cent, as read on the Dare hemoglobinometer, and in many of them it was much lower. In many cases the associated infection as much as or more than the anemia was the indication for transfusions. Medicinal and dietary treatment for marked secondary anemia associated with infection is most discouraging in early childhood, but the condition responds rapidly to these small transfusions.

The next largest group of transfusions was done on patients with septicemia and toxemia, while relatively few were done on new-born and premature infants.

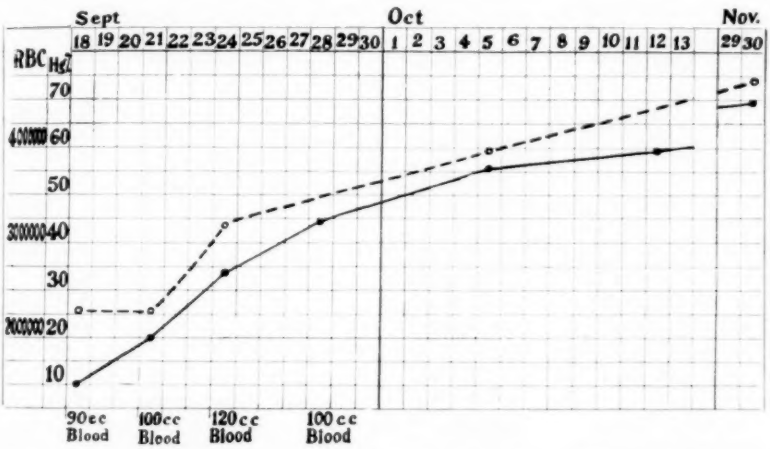

Fig. 3 (case 1).—Extreme degree of secondary anemia of nutritional origin. The rapidity of recovery indicates that intraperitoneally injected blood constitutes a true transfusion.

Five children had primary anemia (table 2), the transfusions in these cases being done as a matter of interest or in the hope that the diagnosis might be wrong.

REPORT OF CASES

To illustrate the therapeutic response to this type of transfusion, the following cases have been selected.

CASE 1.—The mother of a girl, aged 10 months, one of twins, was not well during pregnancy. The infants were born somewhat prematurely. They did not receive proper subsequent feeding. This infant had never had cod liver oil, but did receive ultraviolet light treatments for quite a while. She had marked anorexia and evident rickets. The most extreme pallor possible was present. The hemoglobin was nearly 10 per cent in the Dare scale. The diagnosis was secondary

anemia due to dietary deficiency. Rapid and continued improvement followed intraperitoneal transfusion. The rapidity of recovery indicated that the intraperitoneal blood must have been taken into the blood stream. Reactions to the transfusions did not occur.

Case 2.—A boy, aged 1 year, was breast fed for five months, but after that received practically nothing but milk. Two months before we saw him, he had a severe attack of bronchitis and otitis media. The ear was still discharging when

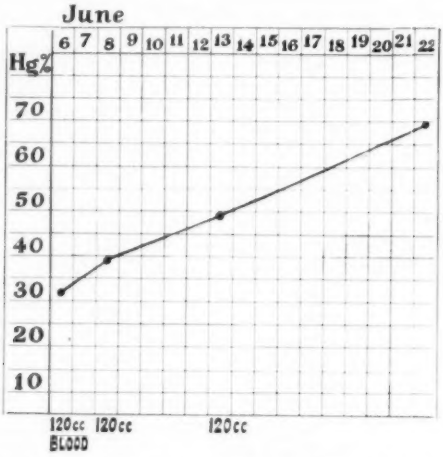

Fig. 4 (case 2).—Severe secondary anemia of nutritional origin, complicated by infections.

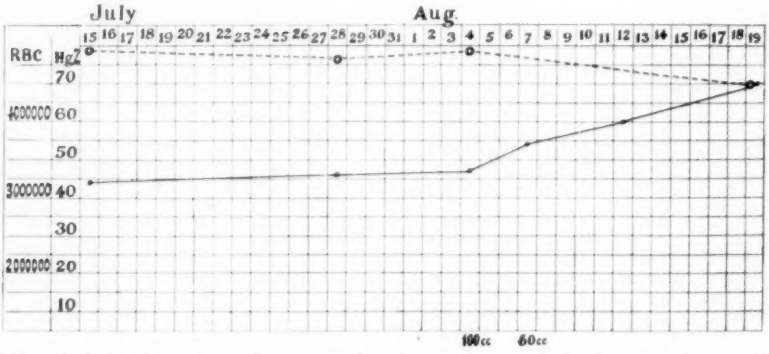

Fig. 5 (case 3).—Secondary anemia of dietary and infectious origin showing slow improvement under dietary and medicinal treatment, but rapid recovery after two small intraperitoneal transfusions.

we saw him. He had marked anorexia. The diagnosis was secondary anemia due to dietary insufficiency and infection.

Case 3.—The mother of a girl, aged 10 months, had toxemia during the later part of pregnancy. The infant had been born one month before term. She had several mild respiratory infections. Her diet had always been carefully supervised and she had received cod liver oil, orange juice and heliotherapy; however, she had

TABLE 3.—*Infants with Secondary Anemia Caused by Infection*

No.	Age	Date	Diagnosis	Amount	Reaction	Result
7680	2 yrs.	3/ 6/27	Mastoiditis	120 cc.	None	Recovered
8604	9 mos.	9/28/25	Otitis media	100 cc.	None	Recovered
7848	2 mos.	1/22/26	Otitis media;	100 cc.	None	
		1/26/26	pneumonia	100 cc.	None	
		1/29/26		100 cc.	None	Recovered
8435	1 yr.	8/30/26	Chronic pneumonia; otitis	80 cc.	None	Recovered
9372	10 mos.	6/ 9/27	Tuberculous pneumonia	120 cc.	None	Died; no postmortem
7940	3 mos.	4/22/26	Pertussis; pneumonia; mastoiditis	100 cc.	Distention	Recovered
7940½	4½ yrs.	2/21/27	Mastoiditis; secondary hemorrhage	90 cc.	None	Recovered
8891	10 mos.	1/17/27	Furunculosis;	100 cc.	None	
		1/19/27	athrepsia;	100 cc.	None	
		1/22/27	syphilis (?)	100 cc.	None	
		2/ 8/27		100 cc.	None	
		2/10/27		100 cc.	None	
		2/12/27		100 cc.	None	
		2/14/27		100 cc.	None	
		2/24/27		100 cc.	None	Recovered
9360	4 mos.	5/28/27	Athrepsia; spastic diplegia	120 cc.	None	
		6/15/27		120 cc.	None	
		6/17/27		120 cc.	None	Recovered
8756	14 mos.	11/13/26	Dysentery	120 cc.	None	
		11/16/26		130 cc.	None	Recovered
1318	4 mos.	4/22/25	Pneumonia; otitis	120 cc.	None	Recovered
		4/29/25		75 cc.	None	
8912	6 mos.	3/19/27	Otitis media;	120 cc.	Severe shock	
		3/23/27	adenitis	120 cc.	Slight	
		3/31/27		80 cc.	Slight	Recovered (dextrose in citrate solution)
7387	6 wks.	1/26/27	Jaundice	120 cc.	Slight	
		1/28/27		120 cc.	None	
		2/ 2/27		120 cc.	None	Recovered
8782	3 yrs.	2/18/27	Mastoiditis	120 cc.	None	Recovered
5671	1 yr.	6/25/26	Mastoiditis	125 cc.	None	
		6/28/26		100 cc.	None	
		7/ 3/26		100 cc.	None	Recovered
7041	1½ yrs.	1/26/27	Otitis media; cervical adenitis	120 cc.	None	
		1/29/27		120 cc.	None	Recovered
7789	9 mos.	12/30/25	Otitis media	90 cc.	None	
		1/ 5/26		90 cc.	None	Recovered
7190	1 yr.	2/19/27	Mastoiditis	120 cc.	None	Recovered
8243	2 yrs.	4/25/27	Cervical adenitis;	120 cc.	None	
		4/30/27	pyelitis	120 cc.	None	Recovered
7679	1 yr.	9/23/25	Intestinal intoxication	75 cc.	Severe	
		11/ 2/25		100 cc.	None	Recovered
7910	1 yr.	5/ 4/26	Pyelitis	100 cc.	None	
		5/ 9/26		100 cc.	None	Recovered
9048	2 yrs.	3/15/27	Pyelitis	100 cc.	None	
		3/22/27		100 cc.	None	Recovered
8093	1 mo.	2/ 3/27	Athrepsia; pneumonia; otitis media	100 cc.	None	Recovered
		2/ 6/27		120 cc.	None	Recovered
8592	1 yr.	12/20/26	Otitis media	80 cc.	None	
		12/27/26		125 cc.	None	Recovered
6391	10 mos.	2/25/26	Mastoiditis	110 cc.	None	
		2/27/26		120 cc.	None	
		3/ 1/26		120 cc.	None	Recovered
8071	1½ yrs.	8/27/27	Pyelitis	120 cc.	None	
				120 cc.	None	Recovered
6102	8 mos.	4/29/26	Mastoiditis;	120 cc.	None	
			erysipelas	120 cc.	None	Recovered
		5/ 1/26		120 cc.	None	Recovered
8211	4 yrs.	4/20/26	Unresolved pneumonia; otitis media	120 cc.	None	
				120 cc.	None	Recovered
9027	4 mos.	3/ 6/27	Athrepsia; mastoiditis	120 cc.	None	
		3/10/27		120 cc.	None	
		3/30/27		120 cc.	None	Died
9643	2 mos.	9/21/27	Diarrhea; acidosis	120 cc.	None	Recovered

TABLE 3.—*Infants with Secondary Anemia Caused by Infection—Continued*

No.	Age	Date	Diagnosis	Amount	Reaction	Result
Fisher I	2 yrs.	Oct. 26	Diarrhea	120 cc. 120 cc.	None None	Recovered
Fisher II	3 yrs.	Oct. 26	Diarrhea	120 cc.	None	Recovered
8747	10 mos.	11/ 7/26 11/11/26 11/16/26	Pyelitis	100 cc. 100 cc. 100 cc.	Slight None None	Recovered
6123	2 yrs.	3/27/25	Influenza	120 cc.	None	Recovered
5712	3 yrs.	3/ 2/27	Mastoiditis	100 cc.	None	Recovered
8970	3 mos.	2/15/27	Syphilis	100 cc.	None	Recovered
8935	4 mos.	5/16/26	Lung abscess; otitis media	100 cc.	None	Recovered
7366	10 mos.	5/13/28	Otitis media; cervical adenitis	120 cc.	None	Recovered
7390	8 mos.	7/ 6/27	Furunculosis; otitis media	120 cc.	None	Recovered
7309	11 mos.	4/21/25 4/23/25	Mastoiditis	60 cc. 75 cc.	None None	Recovered
8178	2 yrs.	4/19/26 4/27/26	Mastoiditis; cervical adenitis	100 cc. 100 cc.	None Slight	Recovered
8618	4 mos.	9/29/26 10/ 6/27	Athrepsia; otitis media	85 cc. 90 cc.	Slight None	Recovered
8975	6 mos.	1/28/27	Mastoiditis; septicemia	120 cc	None	Died
7491	1 yr.	3/16/26	Scarlet fever; mastoiditis	100 cc.	None	Recovered
9411	2 mos.	6/30/27	Otitis media	100 cc.	None	Recovered
7655	4 yrs.	4/27/25 4/29/25	Chronic pneumonia	120 cc. 120 cc.	None None	Recovered
6539	4 yrs.	5/ 3/28	Scarlet fever; mastoiditis; adenitis	120 cc.	None	Recovered
7985	7 mos.	3/30/26 4/ 5/26	Pneumonia; otitis media	60 cc. 120 cc.	None None	Recovered
7548	2 yrs.	1/27/27 1/31/27	Scarlet fever; otitis media	120 cc. 120 cc.	None None	Recovered
9614	2 mos.	10/ 7/27	Syphilis	120 cc.	None	Recovered

become progressively pale. During the first three weeks (table 4), the infant received liver every day. Prompt recovery with continued improvement occurred after two intraperitoneal transfusions of blood.

CASE 4.—In a new-born infant, aged 9 days, a large cephalematoma was opened and drained by the attending physician. On the first day, the child was extremely dehydrated and pale and nearly moribund. The condition of the scalp prevented intrasinus transfusion. Superficial veins were not available. Four ounces (118 cc.) of the father's blood and 2 ounces (59 cc.) of saline solution were injected into the peritoneum. The next day the infant was enormously improved. At the end of one week it looked like a normal child. The diagnosis was secondary anemia due to hemorrhage.

CASE 5.—A girl, aged 13 months, had been on an inadequate diet. She had had mumps at 11 months. She had eaten considerable paint from a bed and chair. The skin was lemon yellow; the spleen was large, and the feet were edematous. Marked basophilic stippling was present. The diagnosis was secondary anemia with probable lead poisoning. The response to transfusion was delayed because of toxemia.

CASE 6.—A girl, aged 4 years, who had always been well previously, had severe cellulitis of the leg from an infected insect bite. The condition spread rapidly

TABLE 4.—*Infants with Secondary Anemia of Nutritional Origin*

No.	Age	Date	Diagnosis	Amount	Reaction	Result
8612	3 mos.	9/28/26	Athrepsia	100 cc.	None	Recovered
		10/ 5/26		100 cc.	None	
8495	2 mos.	8/23/26	Athrepsia	90 cc.	None	
		8/26/26		50 cc.	None	
		8/30/26		100 cc.	None	Recovered
8099	3 mos.	3/22/26	Athrepsia	100 cc.	None	Recovered
7601	1 yr.	7/14/27	Rickets	100 cc.	None	Recovered
10008	15 mos.	3/ 1/27	Mastoiditis	120 cc.	None	
		3/ 3/27		120 cc.	None	Recovered
9218 (Case 5)	1 yr.	4/12/27	Lead poisoning	85 cc.	None	
		4/13/27		100 cc.	None	
		4/15/27		100 cc.	None	
		4/16/27		100 cc.	None	
		4/18/27		100 cc.	None	
		4/20/27		100 cc.	None	
		4/22/27		150 cc.	None	Recovered
9381	3 mos.	6/ 6/27	Pyloric stenosis; athrepsia	60 cc.	None	Recovered
6867 Twin A	10 mos.	3/27/25	Rickets; tetany	120 cc.	None	
		3/30/25		120 cc.	None	
		4/ 7/25		60 cc.	None	
		4/11/25		120 cc.	None	Recovered
6867 Twin B	10 mos.	3/27/25	Rickets; tetany	120 cc.	None	
		3/30/25		120 cc.	None	
		4/ 7/25		60 cc.	None	
		4/11/25		120 cc.	None	Recovered
5216	16 mos.	1/ 7/26	Rickets	90 cc.	None	
		1/12/26		90 cc.	None	Recovered
9370 (Case 2)	11 mos.	6/ 6/27	Rickets	120 cc.	None	
		6/ 8/27		120 cc.	None	
		6/13/27		120 cc.	None	Recovered
9724	6 mos.	11/21/27	Rickets	100 cc.	Slight	
		11/26/27		100 cc.	None	
		12/ 1/27		100 cc.	None	Recovered
7702	4 mos.	9/30/25	Athrepsia; diarrhea	120 cc.	None	Recovered
10182	1 yr.	4/ 6/28	Rickets	140 cc.	None	Recovered
7851	9 mos.	1/ 2/26	Rickets	90 cc.	None	
		1/ 5/26		90 cc.	None	
		1/14/26		90 cc.	None	Recovered
7733	7 mos.	10/22/25	Rickets	90 cc.	None	Recovered
6872	2 yrs.	10/24/25	Rickets	100 cc.	None	Recovered
8596 Twin A (Case 1)	11 mos.	10/12/26	Rickets	100 cc.	None	Recovered
8596 Twin B	11 mos.	9/18/26	Rickets	90 cc.	None	
		9/21/26		100 cc.	None	
		9/24/26		120 cc.	None	
		9/28/26		100 cc.	None	Recovered
8706	10 mos.	11/17/26	Rickets; scurvy	100 cc.	None	Recovered
4828 (Case 3)	10 mos.	8/ 5/26	Rickets	100 cc.	None	
		8/ 7/26		60 cc.	None	Recovered
9162 Twin A	3 mos.	6/17/27	Rickets	100 cc.	Slight	
		6/21/27		120 cc.	None	Recovered
9162 Twin B	3 mos.	6/17/27	Rickets	100 cc.	None	Recovered
7415	2 mos.	6/15/25	Intestinal polyp; hemorrhage	60 cc.	None	
		7/29/25		60 cc.	None	
		8/ 1/25		40 cc.	None	Recovered
6491	3 mos.	12/22/25	Hemorrhage from circumcision	85 cc.	None	
		12/24/25		100 cc.	None	
		12/26/25		100 cc.	None	Recovered
7736	1 yr.	10/30/25	Athrepsia	100 cc.	None	
		11/ 3/25		100 cc.	None	Recovered
6840	10 mos.	5/12/25	Athrepsia; diarrhea	100 cc.	Slight	
		5/15/25		100 cc.	Slight	
		5/18/25		100 cc.	None	Recovered

TABLE 5.—*Data on New-Born and Premature Infants*

No.	Age	Date	Diagnosis	Amount	Reaction	Result
7326	23 days	4/19/25	Sepsis neonatorum....	40 cc.	None	Recovered
6318	5 days	11/30/25	Hemorrhage after circumcision	75 cc.	None	
		12/ 8/25		60 cc.	None	
		12/14/25		60 cc.	None	Recovered
8879	9 days	1/10/27	Hemorrhage after cephalematoma	125 cc.	None	
(Case 4)		1/11/27		120 cc.	None	
		1/13/27		120 cc.	None	Recovered
Quinlan	1 day	3/18/26	Melena.....	60 cc.	None	Recovered
7848	2 days	12/13/25	Melena.....	60 cc.	None	
		12/15/25		100 cc.	None	Recovered
9053	15 days	2/ 8/27	Premature; pylorospasm	110 cc.	None	
		2/12/27		120 cc.	None	
		2/17/27		120 cc.	None	Died; no postmortem
9510	10 days	7/14/27	Premature.....	80 cc.	Slight	Died; no postmortem
9975	2 wks.	1/ 7/28	Diarrhea; athrepsia...	50 cc.	None	Recovered

TABLE 6.—*Data on Infants with Septicemia and Toxemia*

No.	Age	Date	Diagnosis	Amount	Reaction	Result
6557	3 yrs.	1/24/26	Mastoiditis; pneumonia.....	100 cc.	None	
		1/27/26		100 cc.	None	Recovered
Adams	2½ yrs.	2/27/27	Empyema.....	120 cc.	None	Recovered
7817	1 yr.	3/ 8/26	Mastoiditis; septicemia.....	120 cc.	None	Died; no postmortem
8983	1 yr.	1/17/28	Septicemia.....	120 cc.	Slight	
		1/19/28		120 cc.	Slight	Died; no postmortem
9176	6 wks.	3/21/27	Erysipelas; otitis media.....	90 cc.	None	Died
8484	16 mos.	8/23/26	Erysipelas; septicemia.....	100 cc.	Severe	Died; no postmortem
5580	6 mos.	12/20/25	Otitis media; erysipelas.....	90 cc.	None	
		12/21/25		75 cc.	None	Recovered
9061	6 mos.	3/28/27	Pneumonia; otitis media.....	120 cc.	None	Recovered
6982	10 mos.	3/ 4/27	Mastoditis; septicemia.....	100 cc.	None	
(Case 7)		3/16/27		120 cc.	None	Recovered
6540	4 yrs.	4/27/26	Erysipelas; mastoiditis.....	100 cc.	None	Recovered
8223	18 mos.	4/12/28	Mastoiditis.....	120 cc.	None	Recovered
9059	2 yrs.	2/19/27	Pneumonia; otitis media.....	120 cc.	None	Recovered
7367	2 yrs.	7/ 2/26	Mastoiditis.....	125 cc.	None	Recovered
9322	2 wks.	9/11/27	Prematurity; pneumonia; esophageal stricture	45 cc.	None	
		9/14/27		45 cc.	None	
		9/18/27		50 cc.	None	Died; postmortem; abdomen normal
8363	6 mos.	9/ 1/26	Erysipelas; cervical adenitis....	100 cc.	None	
		9/20/26		100 cc.	None	Recovered
8104	1 yr.	4/ 9/26	Mastoiditis; cervical adenitis...	120 cc.	None	Recovered
6860	1 yr.	3/20/27	Mastoiditis; noma; septicemia..	100 cc.	Slight	
		3/24/27		100 cc.	None	
		4/15/27		120 cc.	None	
		4/23/27		120 cc.	None	Died; postmortem; abdomen normal
6819	2 mos.	7/18/24	Erysipelas.....	75 cc.	None	
		7/20/24		75 cc.	None	Recovered
7839	1 yr.	12/25/25	Erysipelas.....	200 cc.	Some	Died; no postmortem
8890	2 yrs.	1/20/27	Septicemia.....	100 cc.	None	
		1/21/27		100 cc.	None	Died; postmortem; abdomen normal
7785	2 yrs.	4/23/26	Mastoiditis.....	100 cc.	None	Recovered
7606	3 yrs.	4/ 4/26	Mastoiditis; erysipelas.....	120 cc.	None	
		4/ 9/26		120 cc.	None	
		4/13/26		120 cc.	None	
		4/19/26		120 cc.	None	Died; no postmortem
9064	4 yrs.	2/15/27	Intestinal intoxication.....	120 cc.	None	Recovered
9404	2 mos.	6/14/27	Pertussis; pneumonia.....	60 cc.	None	
		6/16/27		75 cc.	None	Died; no postmortem
3742	4 yrs.	7/15/27	Cellulitis of leg.....	120 cc.	None	Recovered
(Case 6)						
McDonald	4 mos.	1/14/28	Septicemia.....	120 cc.	None	
		1/16/28		120 cc.	None	Recovered
9988	3 mos.	1/20/28	Erysipelas.....	100 cc.	None	Died; no postmortem

with marked septic fever and extreme prostration. Transfusion was done on the fifth day of the infection. There was immediate cessation of the septic temperature and toxic symptoms with localization of infection. Prompt recovery occurred after drainage of the abscess.

Case 7.—A boy, aged 10 months, who had been well previously except for moderate rickets, was admitted to the hospital toward the end of an attack of

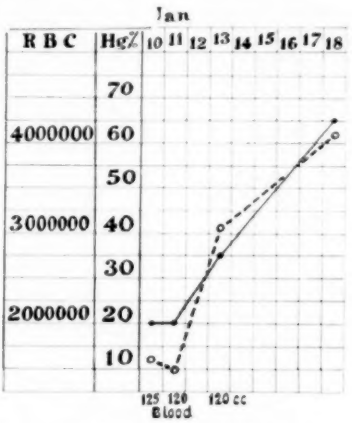

Fig. 6 (case 4).—Extreme anemia due to hemorrhage in the newborn with rapid recovery following intraperitoneal transfusion.

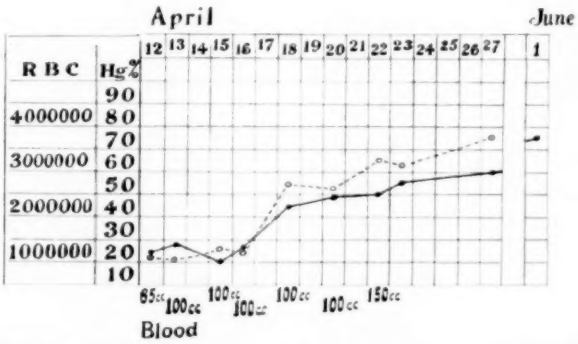

Fig. 7 (case 5).—Secondary anemia due to lead poisoning. Repeated transfusions were given, and recovery was delayed because of toxemia.

pneumonia. A few days later he developed otitis media, followed by severe bilateral mastoiditis. He was extremely sick and toxic during this period. Transfusion was performed preparatory to operation. He was better after drainage of the mastoid but soon developed septic temperature, symptoms of involvement of the joints and orchitis. A roentgenogram of the chest showed nothing of importance. Blood culture was negative. Following the transfusion the temperature dropped to normal, and uninterrupted convalescence took place.

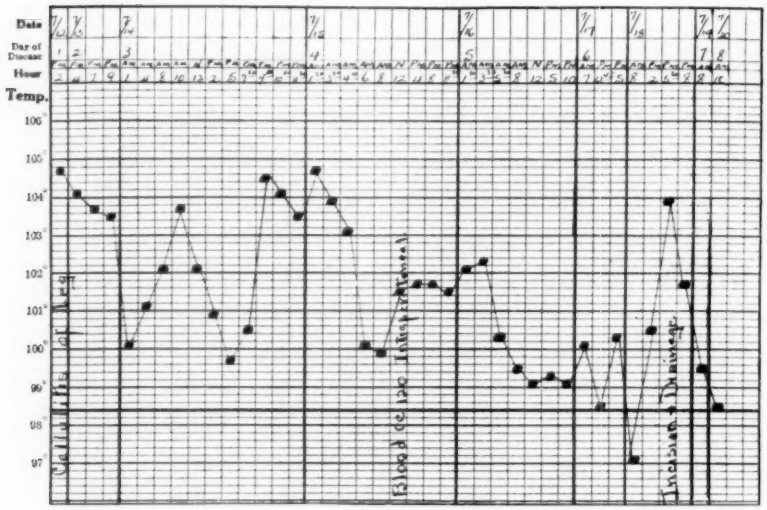

Fig. 8 (case 6).—Severe cellulitis. Prompt cessation of septic temperature and localization of infection following transfusions.

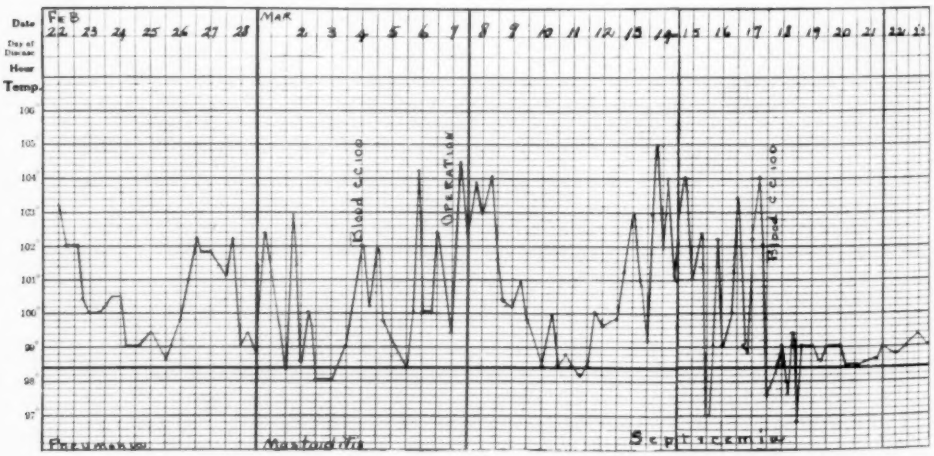

Fig. 9 (case 7).—Pneumonia followed by mastoiditis and septicemia. A critical fall occurred in the temperature after intraperitoneal transfusion.

COMMENT

It is not our purpose in this paper to discuss the value of blood transfusion, but these cases are presented to show that as satisfactory a therapeutic result is obtained by the intraperitoneal method as could be expected by the intravenous.

Reactions in our series occurred in less than 7 per cent of the cases, and in only two or three cases were they of noticeable importance. These reactions usually consisted of restlessness and abdominal discomfort but were rarely accompanied by fever. Proper citration of the blood prevents most of these reactions. As these transfusions were all performed in private practice, in nearly every case the parents of the child were the judges of the reactions, which is fairly good evidence that they were minimal. Certainly, the marked reactions which are rather commonly seen after the intravenous method is used occur much less often after intraperitoneal transfusions.

In the entire series we have never had evidence of injury to any abdominal organ, nor have we experienced anything which could be regarded in any way as an unfavorable effect from the intraperitoneal injection.

Twenty of these patients died, and three came to autopsy. In one case, some unabsorbed blood was found in the abdomen, but this patient was dying when the transfusion was given.

The small amount of disturbance to the patient which these transfusions cause is worthy of mention. Often the crying and struggling which occur when a needle is put into a child's vein and kept there are sufficient to be decidedly harmful. This is greatly minimized by the intraperitoneal method.

The contraindications for intraperitoneal transfusion are the same as for any other type of transfusion with the addition that it should never be used when there is any question of intra-abdominal disease, or when any, even temporary, abdominal discomfort might be disadvantageous, as in severe cardiac disease or acute pneumonia. It has little use, of course, in the rapid replacement of blood volume in shock or hemorrhage, and the hemostatic effect is probably delayed. In every other respect it possesses all of the advantages of intravenous transfusion with the additional advantages of reduced reaction and easy administration. It finds its greatest usefulness in the treatment for secondary anemia and in the combating of infection.

We do not wish to give the impression that we think the intraperitoneal method the best form of transfusion. Unquestionably, the direct method has several advantages not found in any of the citrate methods, but only persons of exceptional skill are able to use it in children. Probably, when it can be readily done, the intraveneous citrate

method is to be preferred. Our purpose in this paper is to show that the intraperitoneal method is safe, that it is effective, that it reduces reactions and that, above all, it is so easy of application that every practitioner of medicine should be able to use it, and thus extend the usefulness of this valuable therapeutic agent.

CONCLUSIONS

1. Two hundred and thirty-seven intraperitoneal blood transfusions are reported without evidence of untoward effect.

2. Intraperitoneal transfusion has all the advantages of intravenous transfusion, except the replacement of blood volume.

3. Reactions are minimized.

4. The method is so simple that every physician should be able to use it.

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THE EFFECT OF DIPHTHERIA TOXIN ON THE ACTION OF INSULIN

A STUDY OF THE EFFECT OF INFECTIONS ON CARBOHYDRATE METABOLISM IN DIABETES MELLITUS*

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Since the introduction of insulin and the work done at the University of Michigan Hospital in 1922, great interest has been taken in the effect of infection on the dosage of insulin. It was soon learned that the occurrence of measles, chickenpox, influenza or any infection in a diabetic patient, particularly in a child, made it necessary to triple or quadruple the dose of insulin. Cowie and Parsons,[1] in April, 1923, pointed out the effect of infections on the action of insulin. They also suggested that the efficiency of insulin is decreased in the presence of a hyperglycemia. The effect produced by bacteria and their toxins on insulin is not an unexplored field at present, but it is the purpose of this paper to record data and facts regarding this subject found in experimental studies in this laboratory. As many phases of this problem could not be solved satisfactorily, other papers on various phases of insulin were reviewed, and a brief study was made of the subject of insulin from the time of its first appearance in the practice of medicine.

In October, 1922, when Dr. Carlson outlined a program to study the different methods of administration of insulin, little insulin was obtainable. Only general directions were published as to methods of preparation.

Dr. Shaffer and his co-workers at Toronto, in 1922, developed a new method for the isolation of the pancreatic hormone. He furnished N. F. Fisher and his co-workers at the Hull Physiological Laboratory of the University of Chicago with explicit directions as to the preparation of insulin. Fisher published a description[2] in September, 1923, of his method of preparing insulin. After obtaining the pancreatic hormone, he found that it could be divided into toxic and nontoxic, or antidiabetic,

* Submitted for publication, Aug. 3, 1928.

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1. Cowie, D. M., and Parsons, J. P.: Clinical Observations on the Use of Insulin in the Treatment of Diabetes in Adults and Children with Particular Reference to the State of Hyperinsulaemia; a Consideration of Insulin and Renal Glycosuria, Tr. Am. Pediat. Soc. **35**:217 (April 30) 1923.

2. Fisher, N. F.: Preparation of Insulin, Am. J. Physiol. **67**:57 (Dec. 1) 1923.

fractions. Fisher concluded that the pancreas contained two antagonistic substances: One substance, called the toxic fraction, raised the amount of sugar in the blood and caused death in rats and guinea-pigs, by excessive stimulation of the medullary centers. The other material, called the active fraction (insulin), was the specific antidiabetic substance. He also concluded that the yield of insulin per kilogram of pancreas is proportional to the degree to which the toxic fraction is removed, and that the toxic fraction seems to cause the irritation and sterile abscesses produced at the sites of injection.

In another paper,[3] published in November, 1923, Fisher asserted that the insulin probably did not represent the entire pancreas hormone complex, since in the total absence of the pancreas, insulin cannot maintain life or control all the diabetic symptoms (subnormal weight, polyphagia and polyuria).

The reports of S. Dietrich on the so-called toxic fraction of the pancreatic hormone were interesting. He described this substance as an insulin-antagonist or "Glykamin".[4] Dietrich's summary on this subject is as follows:

> We have previously communicated that in the blood of diabetic man and epinephrine diabetes, as well as that of hyperglycemic animals, a substance is found denoted by us as Insulinantagonist and which in contrast to insulin considerably hinders the fixation of dextrose through the blood corpuscles. Further we found that this substance, not demonstrable in the blood of normal dogs, appears after pancreas extirpation, and in considerable quantity up to the third or fourth day. We further learned that it not only prevented the fixation of dextrose through the blood corpuscle but by perfusion experiments with the isolated frog's liver, the freeing of dextrose was considerably increased. Then both actions, prevention of flow of dextrose into the body cells and the intensifying of the flow of dextrose from the liver, combine in forming a satisfactory hypothesis for the condition of hyperglycemia. We call the insulin antagonizing hormone "Glykamin."

In another article, Dietrich[5] suggested that the liver was the secreting organ of this glycamin:

> It was previously communicated that not only in diabetic man and animals, but also in normal animals, after the oral administration of dextrose, Glycamin (Glykamin) appears in the peripheral venous blood. I have now found that after oral dextrose, at a time when Glycamin is as yet scarcely demonstrable in the peripheral veins and blood from the portal artery, it is already found in the venous blood of the liver. It is thereby evident that the previously formed assumption that the liver is the organ of secretion of Glycamin agrees essentially with the facts.

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3. Fisher, N. F.: Attempts to Maintain Life of Totally Pancreatectomized Dogs by Insulin, Am. J. Physiol. **67**:634 (Feb.) 1924.

4. Dietrich, S.; Hausler, H., und Loewi, A.: Weiteres über den Insulinantagonislischen Steff, Klin. Wchnschr. **6**:856 (April 30) 1927.

5. Dietrich, S.: Ueber das Sekretionsorgan des Glykamins, Klin. Wchnschr. **6**:856 (April 30) 1927.

In an earlier article Dietrich [6] asserted that the action of insulin gave rise to another problem besides that of antagonistic and active factors. He found insulin to be less efficient in a person with a high blood sugar content than in the same person with a more nearly normal blood sugar content. Cowie and Parsons had pointed out this fact; Dietrich, however, offered an explanation. He believed that the absorption of dextrose from the plasma into the erythrocytes was prevented in hyperglycemic diabetes, and that it might be explained on a physicochemical basis.[6] Dietrich [7] also pointed out that not only is the absorption of dextrose into the erythrocytes prevented in hyperglycemic diabetes, but its absorption from plasma mixed with phlorhizin is also prevented—a property likewise acquired after injection of phlorhizin. This inhibition is produced through the addition of insulin in vitro just as it is with plasma obtained from the hyperglycemic form of diabetes. The absorption of dextrose through the liver, moreover, is prevented by perfusion with a solution containing phlorhizin. In contrast to the result in hyperglycemic diabetes, the freeing of dextrose from both erythrocytes and the liver is not significantly advanced with the addition of insulin in vitro; indeed, it is usually somewhat inhibited.

INFLUENCE OF ACUTE INTOXICATION OR OF ELEVATED TEMPERATURE

The body reaction to insulin in relation to the blood sugar has been discussed; equally important is the reaction of the body to sugar, in the presence of an acute intoxication or of elevated temperature.

Tisdall, Drake and Brown [8] reported an investigation into the factors responsible for the delay in the removal of dextrose from the circulation when it is injected intravenously into dogs with diarrhea, infections or acute intoxication. They also investigated the claim, which they assert has been demonstrated, that the production of insulin is in no way decreased in these disturbances of carbohydrate metabolism.

They came to the following conclusions:

1. The subcutaneous administration of large doses of bacterial toxin (diphtheria toxin) in young dogs definitely impairs the ability of the animals to remove injected glucose from the blood stream at the normal rate. (Table 1.)

6. Dietrich, S.: Efficiency of Insulin in the Presence of Hyperglycemia, Arch. f. d. ges. Physiol. **214**:675, 1926.

7. Dietrich, S., and Loewi, O.: Ueber den Phlorkizindindiabetes, Klin. Wchnschr. **6**:313 (Feb. 12) 1927.

8. Tisdall, F. F.; Drake, T. G. H., and Brown, A.: Production of a Lowered Carbohydrate Tolerance in Dogs, Am. J. Dis. Child. **32**:854 (Dec.) 1926.

2. The subcutaneous administration of large doses of a chemical toxin (histamine) in young dogs definitely impairs the ability of the animal to remove injected glucose from the blood stream at a normal rate. (Table 1.)

3. The rapid production of dehydration in young dogs definitely impairs the ability of the animal to remove injected glucose from the blood stream at a normal rate.

4. The impairment in the ability of the animal to remove injected glucose from the blood stream at a normal rate is not the effect of the substance given or of the

TABLE 1.—*Effect of the Previous Subcutaneous Administration of a Bacterial Toxin (Diphtheria) and a Chemical Toxin (Histamine) on the Blood Sugar of Puppies Before and After Administration of 10 Cc. of a 10 per Cent Solution of Dextrose per Pound of Body Weight (Tisdall, Drake and Brown, Toronto)*

Puppy			Percentage of Blood Sugar				Nonprotein Nitrogen	
No.	Weight, Pounds	Substance of Treatment Given	Before Dextrose Was Given	½ Hour After	1 Hour After	1½ Hours After	in Serum, Mg. per 100 Cc.	Condition of Dog
1	14	30 minimum lethal doses of diphtheria toxin 24 hours before the dextrose	0.115	0.353	0.233	0.193	30.7	Toxic
6	8	30 minimum lethal doses of diphtheria toxin 30 hours before the dextrose	0.095	0.368	0.220	0.141	60.0	Toxic
19	12	7.5 minimum lethal doses of diphtheria toxin 72 and 24 hours before the dextrose	0.115	0.332	0.206	0.151	120.0	Toxic
17	12	210 mg. of histamine divided into four doses during the 30 hours before the dextrose	0.112	0.323	0.225	0.129	20.0	Active; almost normal
20	18	405 mg. of histamine divided into four doses during the 30 hours before the dextrose	0.110	0.277	0.148	0.125	26.0	Apparently normal
24	16	150 mg. of histamine divided into five doses during the 30 hours before the dextrose	0.100	0.353	0.211	0.129	18.1	Apparently normal
26	17	245 mg. of histamine divided into four doses during the 12 hours before the dextrose	0.116	0.383	0.298	0.220	42.0	Toxic
27	20	320 mg. of histamine divided into four doses during the 12 hours before the dextrose	0.116	0.356	0.221	0.156	60.0	Toxic

dehydration produced, but is associated with a more profound functional derangement of the cells, commonly called intoxication. (Table 2.)

5. This intoxication may produce its effect on the sugar tolerance values either by an increase in the glycogenalytic function of the body or by an impairment of the ability of the organism to store carbohydrate.

6. Elevation of temperature without any evidence of intoxication not only does not impair the ability of the animal to remove injected glucose from the blood stream but also causes its removal at a more rapid rate than normal.

Puppies were used in these experiments. The dextrose tolerance test consisted of intravenous injections of 10 cc. per pound of body weight of a 10 per cent solution of dextrose.. The blood sugar deter-

minations were made by the Shaffer-Hartman method. The animals fasted for eighteen hours prior to the experiment.

Cowie and Parsons [1] called attention to the effect of infections (measles, chickenpox, etc.) on the consumption of insulin. In some cases, it required three or four times as much insulin to metabolize a given amount of carbohydrate as it did before the infection was present. When the infection subsided, the need for insulin was appreciably reduced, but not always to that of the period preceding infection until after many days had elapsed. They showed that there is not any determining factor for the amount of insulin necessary during an infection. The dose must be governed by the amount of sugar in the blood and in the urine.

In June, 1924, Rabinowitch [9] reported experiments on the influence of infection on the reaction of the diabetic patient to treatment with

TABLE 2.—*Concentration of Blood Sugar in Normal Puppies Before and After the Administration of 10 Cc. per Pound of Body Weight of a 10 per Cent Solution of Dextrose (Tisdall, Drake and Brown, Toronto)*

Number of Dog	Weight of Dog, Pounds	Percentage of Blood Sugar			
		Before Dextrose Was Given	½ Hour After Dextrose	1 Hour After Dextrose	1½ Hours After Dextrose
1	14	0.087	0.173	0.105	0.097
3	8	0.109	0.142	.....	0.115
4	12	0.109	0.135	0.102	0.098
5	15	0.105	0.112	0.098	0.106
6	8	0.085	0.155	0.088	0.090
7	11	0.100	0.095	0.100	0.100
53	7	0.073	0.173	0.090	0.058
54	10	0.095	0.185	0.083	0.112
55	11	0.093	0.188	0.122	0.083
56	11	0.070	0.194	0.100	0.065

insulin. In the cases of diabetes mellitus, complicated by infections, the blood sugar curves obtained following the administration of insulin presented one phenomenon in common, namely, the absence of the characteristic rapid onset and abrupt fall in the amount of blood sugar. It was also noted that in cases of septicemia and severe acidosis enormous doses of insulin brought about a slight reduction in the amount of blood sugar. These observations seemed to show that fever was a prominent factor in preventing the normal reaction of insulin. In other words, this slow response to the the action of insulin was associated with the fever. A similar reaction to insulin was noted in suppurative processes not associated with fever.

Rabinowitch believed that in the presence of an infection, a routine course cannot be followed in establishing the dosage of insulin. Enormous doses may be required. The amount and frequency of

9. Rabinowitch, L. M.: Influence of Infection upon Reaction of Diabetic to Insulin Treatment, Canad. M. A. J. **14**:481 (June) 1924.

administration during the emergency period is determined best by frequent blood sugar determinations.

Tisdall, Drake, and Brown found that if a given amount of dextrose was injected into an animal already in a toxic condition, the amount of blood sugar increased and remained much greater than it did in a normal animal. One might assume that a toxic animal lacked the ability to utilize dextrose in the tissues normally or to store it in the liver, in the form of glycogen. Sweeney [10] explained this effect of toxemia as impairment of ability to store carbohydrate, which he believed to be an impairment of glycogenesis.

Achard and Block [11] pointed out that anaphylactic shock decreased the amount of glycogen in the liver and increased blood sugar. As Tisdall, Drake, and Brown suggested, it was not only the high fever that caused inability to utilize dextrose, but primarily the intoxication which was associated with a profound derangement of body cells. The amount of glycogen in the liver and sugar in the blood might be increased in either intoxication or anaphylactic shock, but the fundamental causes might be different.

More recently, Sweeney [10] considered the effect of toxemia on tolerance for dextrose and on the action of insulin. Daily tests of tolerance for dextrose were made on rabbits in which toxemias had been produced with diphtheria toxin. Two units of insulin were injected daily, fifteen minutes after the administration of dextrose. The degree of toxemia thus produced appeared to have little, if any, effect on the action of the insulin. On the basis of these and preceding experiments, the author suggests that the effect of toxemia is that of a suppression of the endogenous production of insulin.

Sweeney further stated that the principal effect of diphtheria toxin might be assumed to be impairment of ability to store carbohydrates. If the storage of carbohydrates was brought about by endogenous insulin, the toxemia might be thought to have a direct depressing effect on the production of insulin. In his experience, suppressed production of endogenous insulin seemed to be a more plausible explanation than that of an increased glycogenolysis or a disturbed glycogenesis, independent of endogenous insulin. His impression was that the need for more insulin to control the hyperglycemia during the infectious processes might indicate toxic effects on those islands of Langerhans which are still functioning.

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10. Sweeney, J. S., and Lockey, R. W.: The Effect of Toxemia on Tolerance for Dextrose, Arch. Int. Med. **41**:257 (Feb.) 1928.

11. Achard, C., and Block, S.: Anaphylactic Disturbance and Pyemia as a Complication of Insulin Treatment of Diabetic Coma, Bull. et mém. Soc. méd. d. hôp. de Paris **49**:1210 (July 24) 1925.

Zeckwer and Goodell carried Sweeney's work a little farther and injected killed *Bacillus proteus, Bacillus coli* and *Bacillus paratyphosus* into the blood stream of rabbits. They studied the blood sugar changes following the injections. There was a rapid rise in the amount of blood sugar then a return to nearly normal in the course of a few hours.[12]

The work of Lawrence and Buckley[13] of King's College Hospital, London, deals not only with the action of toxemias on the blood sugar and on the action of insulin but with the effect of toxemias and infections on the thyroid and suprarenal glands. The conclusions reached by these men are as follows: A condition may be produced in rabbits with diphtheria toxin in which (*a*) insulin action is reduced or absent; (*b*) a prelethal rise in blood sugar occurs, which has been reduced by ergotamine and is therefore due to glycogenolysis, (*c*) striking and histologic changes have been found in the thyroid and suprarenal glands. It would appear from the reports of Lawrence and Buckley that there is a mechanism in the thyroid and suprarenal glands—the "thyroidadrenal apparatus"—which, when stimulated, is a direct physiologic antagonist to the action of insulin. This mechanism, they asserted, is stimulated by toxemias, and particularly by bacterial infections. If this observation is correct, it seems to explain adequately the increased severity of diabetes, and the failure of insulin action in these conditions.

Since it has been commonly observed that insulin is less efficient when given to experimental animals and diabetic patients with infection and intoxication, it seems reasonable to suppose, in the light of the work of Dietrich, Rabinowitch, Fisher, Lawrence and others, that the low sugar tolerance thus induced is not due to a decrease in the normal secretion of insulin. On the other hand, it is more reasonable to believe that the low sugar tolerance is due to some injury or inhibitory action on the insulin; it may also be due to the inability of the deranged tissue cells to utilize the dextrose.

It was the purpose of this investigation to determine, if possible, whether diphtheria toxin had any effect in overcoming the action of insulin in normal rabbits and, if so, to seek the explanation. If diphtheria toxin injures the insulin normally present in the body, it would seem that insulin incubated with the toxin in a test tube for a certain length of time would become less efficient when injected into the body.

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12. Zeckwer, I. T., and Goodell, H.: Blood Sugar Studies as a Result of Intravenous Injection of Killed Bacteria, J. Exper. Med. **42**:43 (July) 1925.

13. Lawrence, R. D.: Inhibition of Insulin Action by Toxaemias, Brit. M. J. **2**:983 (Nov. 27) 1926.

METHOD

Owing to the fact that a large number of blood sugar determinations were necessary in these experiments, a method was sought which would be relatively accurate with small samples of blood and which would prove more rapid than the Folin-Wu method. A micromethod, a modification of the Folin-Wu method, and devised by several workers at Mt. Sinai Hospital, New York, was chosen, since but 0.1 cc. of blood was necessary for a single determination. A series of comparative tests were conducted with this method and the Folin-Wu method. These are recorded in table 3. It will be seen that the micromethod gave an average variation of 0.0053 per cent below that of the Folin-Wu colorimeter method.

This method is carried out as follows:

TABLE 3.—*Variation in Blood Sugar Determinations by Folin-Wu Method and Micromethod*

Patient	Age	Remarks	Folin-Wu Method, per Cent	Micro-method, per Cent	Variation, per Cent	Average Variation, per Cent
1	.....	.....	0.102	0.092	—0.010	
				0.097	—0.005	
2	26 years	Normal blood	0.098	0.093	—0.005	
			0.097	0.092	—0.005	
3	25 years	Normal blood	0.114	0.109	—0.005	
			0.112	0.102	—0.010	
4	25 years	Normal blood	0.097	0.101	+0.004	—0.0053
			0.096	0.099	+0.003	
5	45 years	Malaria	0.095	0.091	—0.004	
6	45 years	Malaria	0.075	0.073	—0.002	
				0.076	+0.001	
7	46 years	Malaria	0.087	0.089	+0.002	
8	37 years	Malaria	0.097	0.101	+0.004	

One tenth of a cubic centimeter of a 10 per cent solution of sodium tungstate and 0.1 cc. of fresh blood from the rabbit's ear are placed in a graduated 1 cc. tube. The tube is then filled to the 1 cc. mark with N/12 H_2SO_4 and the tube centrifugalized for five minutes. Five tenths of a cubic centimeter of the supernatant fluid and 0.5 cc. of alkaline Folin-Wu copper solution are placed in a test tube graduated to 5 cc.; this is boiled for six minutes. Five tenths of a cubic centimeter of Folin-Wu phosphomolybdate solution is now added, and the tube is filled with distilled water to the 5 cc. mark. One cubic centimeter of this solution is placed in a Sahli hemoglobinometer tube and diluted with distilled water until it matches the standard which was prepared in Mount Sinai Hospital Laboratories, New York.

REPORT OF EXPERIMENTS

EXPERIMENT 1.—*Results of Injection of One-Fifth Unit of Insulin on the Blood Sugar of Rabbits on a Known Standard Diet.*

Rabbits weighing 3 pounds and receiving a standard diet of barley and lettuce were used in the experiments. The diet was so regulated that all of the specified quantity of barley and lettuce was consumed at each feeding. After the injection of one-fifth unit of insulin subcutaneously, the amount of blood sugar

would drop from normal figures varying between 0.095 and 0.1 per cent (table 4) to a fairly constant level of 0.045 per cent (table 5). This experiment was repeated on different rabbits, and the results were approximately the same (tables 4 and 5). The amount of blood sugar reached its lowest point one hour after injection and usually returned to the normal level in from three to four hours.

TABLE 4.—*Amount of Blood Sugar in Normal Rabbits on Standard Diet Measured by the Micromethod*

Date	Rabbit Number	Determination 1, per Cent	Determination 2, per Cent	Variation	Average, per Cent	Average Percentage of Blood Sugar for Fourteen Determinations
9/20/26	4	0.095	0.097	0.002	0.096	
9/21/26	4	0.082	0.088	0.007	0.085	
9/21/26	4	0.080	0.079	0.001	0.0795	
9/22/26	4	0.081	0.085	0.004	0.083	
9/25/26	4	0.090	0.092	0.002	0.091	
9/27/26	4	0.110	0.105	0.005	0.1075	
10/ 5/26	4	0.110	0.111	0.001	0.1106	
10/ 7/26	4	0.105	0.105	0.000	0.105	0.093
12/ 8/26	5	0.083	0.090	0.007	0.0865	
12/ 9/26	6	0.086	0.089	0.003	0.0875	
12/10/26	6	0.078	0.083	0.005	0.0805	
12/11/26	7	0.086	0.088	0.002	0.087	
1/ 5/27	8	0.089	0.090	0.001	0.0896	
1/15/27	8	0.096	0.092	0.003	0.0935	

TABLE 5.—*Effect of Insulin on the Percentage of Blood Sugar and the Condition of Fasting Rabbits Previously Kept on a Standard Diet*

Interval of Time, Hours	Rabbit 4		Rabbit 5		Rabbit 6		Rabbit 7	
	Per Cent	Remarks	Per Cent	Remarks	Per Cent	Remarks	Per Cent	Remarks
0	0.090	.....	0.088	.....	0.105	.....	0.092	.....
¼	.....	⅛ unit of insulin	.....	⅛ unit of insulin	.....	⅜ unit of insulin	.....	⅜ unit of insulin
½	0.070	Normal	0.066	Normal	0.069	Normal	0.060	Irritable
¾	0.068	Normal	.....	Normal	.....	Irritable	.....	Convulsions
1	0.045	Normal	0.046	Normal	0.043	Irritable	0.025	Convulsions
1½	0.047	Normal	0.045	Normal	.....	Convulsions	0.025	Convulsions
2	0.047	Normal	0.046	Normal	0.031	Convulsions	0.027	Convulsions
3	0.055	Normal	0.061	Normal	0.036	Convulsions	0.045	Irritable
4	0.070	Normal	0.080	Normal	0.040	Convulsions	.....	Irritable
5	0.077	Normal	0.085	Normal	0.045	Irritable	0.065	Normal
6	0.081	Normal	0.084	Normal	0.049	Irritable	0.087	.....
7	0.089	.....	.....	.....	0.056	Normal	.....	.....
14½	.....	.....	.....	.....	0.095	Normal	.....	.....

EXPERIMENT 2.—*Effect of One-Fifth Unit of Insulin, After Incubation at 37 C. for Eighteen Hours Before Injection, on the Amount of Blood Sugar in Normal Rabbits on a Standard Diet.*

In this experiment, the insulin was incubated at body temperature for eighteen hours before it was injected subcutaneously. Table 6 indicates little or no difference in the results from those in the control series (table 5). This would seem to show that incubation of insulin for eighteen hours at 37 C. does not have any material effect on its efficiency.

EXPERIMENT 3.—*Effect of the Injection of Three Minimum Lethal Doses of Diphtheria Toxin on the Blood Sugar of Normal Rabbits.*

Three minimum lethal doses of diphtheria toxin, determined by injections in guinea-pigs, were injected subcutaneously into three normal rabbits. Blood sugar estimations were made at more or less definite intervals for thirty and one-half

TABLE 6.—*Effect Produced by Injection of Insulin Which Has Been Incubated for Eighteen Hours on the Amount of Blood Sugar in Normal Rabbits on a Standard Diet*

Intervals of Time, Hours	Rabbit 4	Rabbit 5	Rabbit 6
0	0.096%	0.090%	0.100%
¼	⅛ unit of insulin subcutaneously	⅛ unit of insulin subcutaneously	⅛ unit of insulin subcutaneously
½	0.073%	0.065%	0.066%
¾	0.069%	0.063%	0.063%
1	0.047%	.....	0.045%
1½	0.046%	0.044%	0.047%
2	0.049%	0.047%	.....
3	0.058%	0.060%	0.062%
4	0.074%	0.081%	0.075%
5	0.080%	0.088%	0.084%
6	0.088%	0.095%	0.090%

TABLE 7.—*Effect of Diphtheria Toxin on Fasting Rabbits Previously Kept on a Known Restricted Diet*

	Rabbit 5		Rabbit 6		Rabbit 8	
Time in Hours	Blood Sugar, per Cent	Remarks	Blood Sugar, per Cent	Remarks	Blood Sugar, per Cent	Remarks
0	0.090	.....	0.089	.....	0.083	.....
¼	3 minimum lethal doses of diphtheria toxin, subcutaneously, incubated for 18 hours		3 minimum lethal doses of diphtheria toxin, subcutaneously, incubated for 18 hours		3 minimum lethal doses of diphtheria toxin, subcutaneously, incubated for 18 hours	
1¼	0.092	.....	.....	.....	0.080	.....
2¼	0.089	.....	.....	.....	0.080	.....
3¼	0.087	.....	0.090	.....	0.081	.....
4¼	0.092	.....	.....	.....	.....	.....
5¼	0.083	.....	.....	.....	.....	.....
6½	.....	.....	0.087	.....	.....	.....
7	.....	.....	.....	.....	.....	.....
8	.....	.....	.....	.....	.....	.....
9	.....	.....	0.086	.....	0.084	.....
30½	0.083	Toxic	0.083	Toxic	0.079	Toxic
31	.....	20 cc. of 10 per cent dextrose	.....	Toxic	.....	Toxic
31½	0.102	.....	0.086	⅛ unit of insulin	0.081	Toxic
31¾	0.110	Toxic	.....	.....	.....	⅛ unit of insulin
32	.....	½ unit of insulin	0.068	Toxic	0.080	Toxic
32½	0.095	.....	.....	Toxic	0.063	Toxic
33	0.092	Toxic	0.070	Toxic	.....	Toxic
33½	0.087	Toxic	.....	Toxic	0.069	Toxic
34	0.088	Toxic	.....	Toxic	.....	Toxic
36	0.090	Toxic	0.085	Toxic	0.078	Toxic
48	.....	.....	0.092	Recovery	.....	Dead

hours, when the rabbits developed the first signs of intoxication (table 7).[14] The determinations were continued at regular intervals following the onset of the symptoms of intoxication. The sugar concentration of the blood remained approxi-

14. The animal was inactive and had an elevated temperature of 102 to 103 F.; its eyes had lost their luster. Respiration was increased, and there was a complete change from the previous active state.

mately normal[15] until signs of intoxication appeared. During the first hour after these symptoms appeared, a slight rise was noted. At this point, one-fifth of a unit of insulin was given subcutaneously to rabbit 6. Half an hour later, there was a definite drop in the blood sugar curve from 0.086 to 0.068 per cent. By the fourth hour after the insulin was given, the blood sugar returned to its former content of 0.085 per cent. Sixteen hours after the insulin was given, the rabbit once more appeared normal. This same experiment was repeated on rabbit 8, and practically the same results for the blood sugar were obtained (table 7). The blood sugar curves in these experiments may be compared with those of the control animals (table 5).

The report for rabbit 5 in table 7 shows again that the efficiency of insulin is impaired considerably by an intoxication. In this experiment, 20 cc. of a 10 per cent solution of dextrose was given intraperitoneally during the toxic state,[16] and the amount of blood sugar rose to 0.110 per cent in two hours. At this point, one-half unit of insulin was injected subcutaneously. An hour after the injection of the insulin, the blood sugar content had dropped only to 0.092 per cent; at the end of two and one-half hours, to 0.087 per cent, and at the end of five hours to 0.090 per cent. The animal, however, still appeared toxic. The amount of blood sugar at no time dropped below normal, following this injection of insulin. If the efficiency of the insulin in this case had not been affected in some way by the intoxication, it seems that it should have reduced the amount of blood sugar to a much lower level, since three fifths of the unit of insulin reduced the blood sugar in the control animal, during the first hour to 0.025 per cent (table 5, rabbit 7).

EXPERIMENT 4 (Greenthal and Brown).—*Effect of Injections of Foreign Protein on the Blood Sugar of Man and Animals.*

At this time, a question arose regarding the effect of foreign protein on the blood sugar and what part it might play in causing a variation in the amount of blood sugar in normal rabbits.

Greenthal and Brown[17] carried out a series of experimental studies in 1922, concerning the nature of nonspecific protein in disease processes. In their experiment, they used six fasting patients who had not been sensitized. Dead typhoid bacilli were injected intravenously, and the effect on the curve for blood sugar was noted. The amount of blood sugar increased slightly during the height of the fever, but quickly returned to normal (Folin-Wu method). Zeckwer and Goodell[12] found that the injection of foreign protein, such as killed bacteria, caused a rapid rise in blood sugar. Achard and Block[11] declared that anaphylactic shock due to foreign protein caused a decrease in the amount of glycogen in the liver and an increase in that in the blood sugar.

EXPERIMENT 5.—*Effect of Horse Serum on the Blood Sugar Curve of a Previously Sensitized Rabbit.*

The rabbits used in this experiment were sensitized to horse serum by two intramuscular injections of the serum, given a week apart. Three weeks after

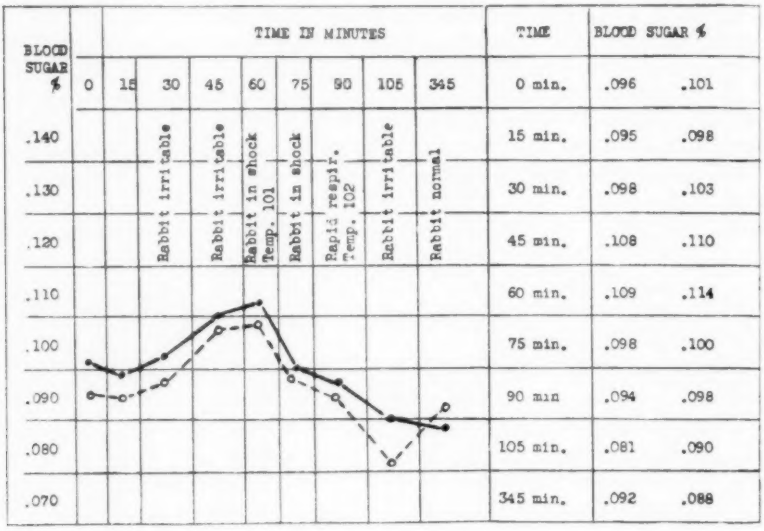
15. Any slight variations in the sugar content that occurred during this period could be explained on the basis of the normal variations of animals fasting from six to ten hours, excitement and experimental manipulation.

16. The toxic state was determined by lassitude, fever of 103 F. per rectum, loss of luster in eyes and increased respiration.

17. Greenthal, R. M., and Brown, G. M.: Studies on the Nature of Non-Specific Protein in Disease Processes, Arch. Int. Med. **30**:99 (July) 1922.

the last injection of serum, the skin of the abdomen was shaved and two drops of the horse serum were injected intramuscularly. In a half hour, a red wheal about the size of a dime, appeared at the site of injection in each of the animals. These animals were then considered sensitized and were studied for the effect of an injection of horse serum on the blood sugar level. The results show that in forty-five minutes after the injection the amount of blood sugar increased and remained elevated for approximately a half hour, as was shown in the studies of Greenthal and Brown in man.[18] Subsequent determinations, however, revealed that the amount of blood sugar dropped below the normal level and did not return to normal for four hours, as shown graphically in table 8. Greenthal and Brown stated that the reason for the increase in amount of blood sugar during the fever, in their experiments, was not clear. They considered that it might be

TABLE 8.—*Effect of Horse Serum on the Blood Sugar Curve of a Previously Sensitized Rabbit: Two Experiments, Each Represented by a Curve*



TIME	BLOOD SUGAR %	
0 min.	.096	.101
15 min.	.095	.098
30 min.	.098	.103
45 min.	.108	.110
60 min.	.109	.114
75 min.	.098	.100
90 min	.094	.098
105 min.	.081	.090
345 min.	.092	.088

the result either of increased metabolism or of stimulation of the glycogen reserve. O'Neill[19] and others supplied the evidence that intense glycogenolysis occurs in anaphylaxis and high temperatures. They showed that a complete disappearance of glycogen from the livers of dogs takes place within fifteen minutes after the onset of those conditions.

In the animals in experiment 5, the drop to subnormal following the brief initial rise in amount of blood sugar may be explained on a slightly different basis. It seems plausible that after a fever has existed for a variable length of time, the mobilized blood sugar burns more rapidly.

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18. Greenthal and Brown used, for their experiments, hospital patients who were being treated with intravenous injections of protein as a therapeutic measure for arthritis, chorea and various infections of the eyes.

19. O'Neill, F. I.; Manwaring, W. H., and Bing, Moy: Quantitative Changes in Hepatic Glycogen in Anaphylactic Shock, J. A. M. A. **74**:1102 (April 11) 1925.

These results led me to investigate the possible effect of fever on the blood sugar content. Through the courtesy of Professor Wile, I was permitted to make some observations on paretic patients in his clinic who were being treated by the induction of malaria fever with the injection of malaria plasmodia.

The following series of experiments shows the relationship between high temperature and the blood sugar level. Of course, other factors than high temperature may be responsible in these cases.

EXPERIMENT 6.—*Effect of High Temperature on Blood Sugar Content (Folin-Wu Method).*

The following determinations were made on patients suffering from a malarial chill:

Patient A showed a normal blood sugar content of 0.095 per cent before the chill, and a normal temperature. During the chill, the temperature rose to 104 F.

TABLE 9.—*Effect of Fever or Malarial Paroxysm on Amount of Blood Sugar in a Patient on a Standard Diet*

		Temperature, F.	Blood Sugar, per Cent
Patient A	No symptoms; temperature normal	98	0.095
	Malarial chill; high fever; chills; weakness and apathy	104	0.075
	Five hours later; no fever; chills subdued; patient weak	98.4	0.087
Patient B	No symptoms; temperature normal	98	0.105
	Malarial chill; high fever; chills; sweats and weakness	104.4	0.080
	Eight hours later; no fever; chills subsided; patient weak	97.2	0.097
Patient C	No symptoms; temperature normal	98	0.090
	Malarial chill; high fever; chills; sweats and weakness; apathy	104.2	0.079
	Twelve hours later; no fever; chills subsided; patient weak	98.2	0.087
Patient D	No symptoms; temperature normal	97.4	0.101
	Malarial chill; chills and sweats; patient apathetic	105	0.078
	Seven hours later; temperature normal	98	0.096

The amount of blood sugar decreased to 0.075 per cent. Five hours after the chill, the temperature was 98.4 F., and the blood sugar content 0.087 per cent.

Patient B, before the febrile period, showed a normal blood sugar content of 0.105 per cent and a temperature of 98 F. During the chill, the temperature reached 104.4 F., and the amount of blood sugar decreased to 0.08 per cent. The patient had severe sweats and marked weakness. Eight hours later, the temperature was normal and the blood sugar amounted to 0.097 per cent.

Two more patients were studied in like manner during a malarial chill, and the same results were obtained (table 9). This experiment shows that the amount of blood sugar is lowered during a febrile period. These patients were studied under uniform conditions; that is, the patients were expected to have a chill, and the meal preceding the experiment was omitted. The sample of blood was taken during the height of the chill.

EXPERIMENT 7.—*Incubation of Three Minimum Lethal Doses of Diphtheria Toxin with One-Fifth Unit of Insulin.*

Three minimum lethal doses of diphtheria toxin were incubated in a test tube with one-fifth unit of insulin for eighteen hours, at body temperature. This mixture was then injected subcutaneously, and blood sugar determinations were made at definite intervals.

When these determinations are compared with those which were made after the injection of insulin alone (table 5), a striking difference is noted. One-half hour after the injection of one-fifth unit of insulin incubated with toxin, the amount of blood sugar was lowered to 0.077 per cent, while in the control it was lowered to 0.061 per cent (this finding was present in all five experiments). This shows that insulin which is incubated with diphtheria toxin in vitro for a sufficient time acts with less than normal rapidity (table 10).

At the end of one hour, the insulin injected alone had reduced the amount of blood sugar to 0.045 per cent (table 5), while the insulin incubated with diphtheria toxin, at the end of an hour, had only reduced the amount of blood sugar to 0.055 per cent, which is an appreciable difference. At the end of the second hour, the blood determination made with untreated insulin was 0.046 per cent, while that of insulin incubated with toxin was 0.07 per cent. At the end of the third hour, the determination made after an injection of untreated insulin was 0.055 per cent, while that of insulin incubated with toxin was normal or 0.09 per cent.

TABLE 10.—*The Effect of the Subcutaneous Administration of a Mixture of Diphtheria Toxin and Insulin, Incubated for Eighteen Hours, on the Amount of Blood Sugar in Rabbits of a Known Weight, on a Standard Diet*

Substance injected: mixture of 1/5 unit of insulin incubated for 18 hours with three minimum lethal doses of diphtheria toxin

Rabbit*		Percentage of Blood Sugar							
No.	Weight, Pounds	Before Mixture Was Given	½ Hour After Mixture	1 Hour After Mixture	2 Hours After Mixture	3 Hours After Mixture	4¼ Hours After Mixture	6 Hours After Mixture	Condition of Rabbit
4	3	0.089	0.075	0.054	0.070	0.090	0.087	0.087	Apparently normal
5	3	0.090	0.077	0.056	0.068	0.092	0.090	0.089	Apparently normal
6	3	0.105	0.074	0.055	0.075	0.095	0.097	0.095	Apparently normal
7	3	0.092	0.080	0.059	0.070	0.088	0.090	0.090	Apparently normal
8	3¼	0.095	0.082	0.054	0.072	0.092	0.098	0.095	Apparently normal

* The animals used in this experiment were on a carefully standardized diet. The minimum lethal dosage was determined on a guinea-pig weighing 250 Gm.

This leads to the conclusion that when insulin is incubated with diphtheria toxin for eighteen hours at 37 C., it becomes less efficient. The amount of blood sugar is not reduced as quickly or as much, and is not decreased as long as when untreated insulin is used (tables 5 and 10).

EXPERIMENT 8.—*The Effect of the Subcutaneous Administration of a Mixture of Diphtheria Toxin and Insulin, Injected Immediately After Mixing, on the Blood Sugar of Rabbits.*

The rabbits were given subcutaneous injections of one-fifth unit of insulin, which had been thoroughly mixed with 3 minimum lethal doses of diphtheria toxin and allowed to stand at room temperature for only fifteen minutes before injection. In this experiment, the curve for blood sugar (table 11) was practically the same as that of the control animals which were given the same amount of untreated insulin (table 5).

COMMENT ON RESULTS

It is clear from the amounts of blood sugar recorded in the tables and the chart, as well as from other results not included, that there is a tendency for the blood sugar during fasting to vary from time to time.

The variations appear to be due to changing activity and experimental manipulation.

Increase in Amount of Blood Sugar with the Onset of a Toxic State.—Diphtheria toxin, which causes an intoxication in thirty hours and a temperature of from 101 to 103 F., causes a slight increase in the amount of blood sugar soon after the signs of intoxication become manifest. This elevation is transient and soon passes off. Mikami [20] has produced practically the same results with the intravenous injection of diphtheria toxin in rabbits. With large doses, a hyperglycemia was produced which gradually decreased as the toxic symptoms progressed. Others [21] have produced similar hyperglycemias with injections of foreign proteins.

TABLE 11.—*The Effect of the Subcutaneous Administration of a Mixture of Diphtheria Toxin and Insulin, Injected Immediately After Mixing, on the Amount of Blood Sugar in Rabbits of a Known Weight and on a Standard Diet.**

Substance injected: ⅛ unit of insulin mixed with three minimum lethal doses‡ of diphtheria toxin, not incubated

Rabbit†		Percentage of Blood Sugar						
No.	Weight, Pounds	Before Drug Was Given	½ Hour After Drug	1 Hour After Drug	2 Hours After Drug	3 Hours After Drug	4¼ Hours After Drug	Condition of Rabbit
4	3	0.087	0.060	0.045	0.049	0.060	0.085	Apparently normal
5	3	0.090	0.061	0.046	0.045	0.057	0.089	Apparently normal
6	3	0.099	0.059	0.045	0.047	0.062	0.097	Apparently normal
7	3	0.093	0.062	0.044	0.046	0.055	0.090	Apparently normal
8	3¼	0.097	0.060	0.046	0.046	0.062	0.095	Apparently normal

* Control curves are given in tables 6, 7 and 10.
† The animals used in this experiment were on a carefully standardized diet.
‡ The minimum lethal dosage was determined on a guinea-pig weighing 250 Gm.

Increase in Amount of Blood Sugar at the Onset of an Allergic Reaction.—The tables show a temporary increase in amount of blood sugar after the injection of 1 cc. of horse serum in a previously sensitized rabbit. Achard, Greenthal, Zeckwer, Sefcik,[22] O'Neill and others produced similar hyperglycemias with injections of foreign proteins in man and animals.[23] O'Neill, Achard and Zeckwer all gave practically the same explanation for this phenomenon. They showed that intense glycogenolysis occurs in anaphylaxis and allergic reactions,

20. Mikami, S.: Tohoku J. Exper. Med. **6**:299, 1925.

21. Achard and Block (footnote 11). Zeckwer and Goodell (footnote 12). O'Neill (footnote 19).

22. Sefcik, J. A.: Action of Protein Injection on Blood Sugar After Administration of Insulin, abstr., J. A. M. A. **82**:1310 (April 19) 1924.

23. Achard and Block (footnote 11). Greenthal and Brown (footnote 17). Zeckwer and Goodell (footnote 12). Menten, M. L., and Manning, H. M.: Blood Sugar Studies on Rabbits Infected with Organisms of the Enteritidis-Paratyphoid B Group, J. M. Research **44**:675, 1924. O'Neill (footnote 19).

as revealed by the partial or complete disappearance of glycogen from the livers of dogs a few minutes after the onset of the reaction. This mobilization of glycogen from the liver results in hyperglycemia.

Decrease in Amount of Blood Sugar During an Intense Malarial Paroxysm of Several Hours' Duration.—The tables disclose that the amount of blood sugar is lowered during an intense malarial paroxysm. This may be due to increased metabolism during a chill, the blood sugar being utilized faster than it can be supplied from the glycogen reserve.[24]

Diminution or Failure of Insulin Action.—The tables and chart show that after the injection of diphtheria toxin and the appearance of signs of intoxication, the hypoglycemic action of insulin is less than before the injection.

Insulin has probably two actions which must be considered in the explanation of the foregoing phenomena. In the first place, it has been definitely shown to form glycogen in the muscles and liver when an abundance of dextrose and insulin is present.[25] It has [illegible] however, to do so with small doses and with little blood sugar to [illegible] on, according to Lawrence and Buckley. A failure to form glycogen, however, is not a likely explanation.

The explanation seems to lie in the action of insulin suggested by Lesser, Dale and others—that it checks the production of new sugar from protein and fat and perhaps from preformed glycogen. When the amount of blood sugar is low, less production of new sugar is going on for insulin to check, and the amount of blood sugar remains constant.

This, however, still does not explain fully why insulin fails to decrease the amount of blood sugar. If it checked the production of new sugar, one would expect the amount of blood sugar to decrease gradually as it is used in tissue metabolism. Lawrence [25] asserted that a certain level of hypoglycemia produced by insulin causes a reactive mobilization of new sugar either directly from the liver glycogen, or more probably through stimulation with epinephrine. He also stated that if the suprarenal gland is overactive, as would seem to be the case after certain degrees of diphtheria poisoning, it may be that the suprarenal reaction is produced more easily and at a higher blood sugar level, and refuses to allow the blood sugar to sink below normal. Lawrence and Buckley showed that toxemias do stimulate the suprarenal and thyroid glands and that the suprarenal-thyroid system does stimulate

24. Riddle,; O. Honeywell, H. E., and Fisher, W. S.: Am. J. Physiol. **68**:461, 1924.

25. Lawrence, R. D., and Buckley, O. B.: Inhibition of Insulin Action by Toxemias and Its Explanation: Effect of Diphtheria Toxin on Blood Sugar and Insulin Action in Rabbits, Brit. J. Exper. Path. **8**:58 (Feb.) 1927.

the mobilization of new sugar and is, thus, a physiologic antagonist to insulin. This, then, seems to be the cause of the failure in the action of insulin during infections in diabetic patients. Riddle [24] also contributed evidence to this statement. He stated that heavy doses of insulin have been shown to cause enlargement of the suprarenal glands in dogs. I advanced the foregoing explanation tentatively, at present, as the most probable explanation of the variation in the action of insulin in the presence of toxic conditions.

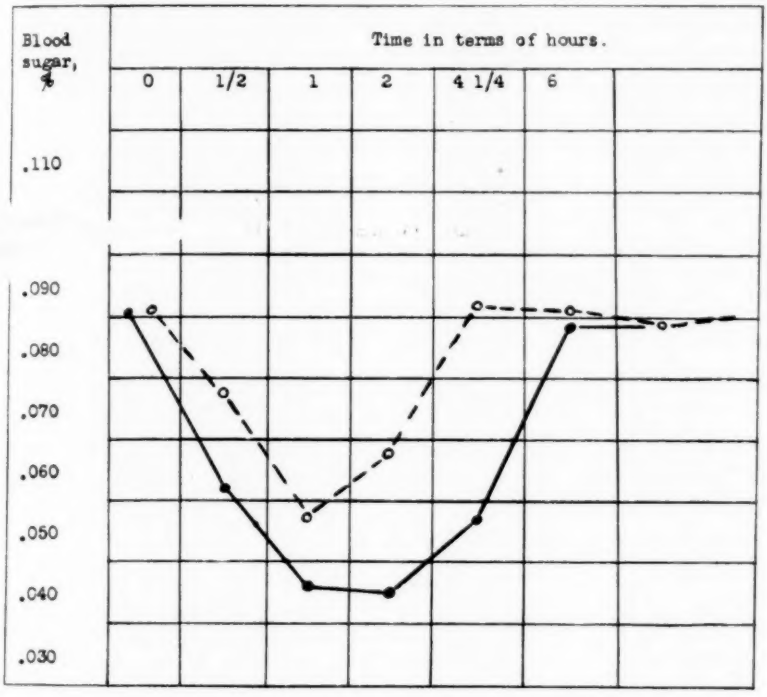

CHART A.

The effect produced on the amount of blood sugar, by the administration of insulin previously incubated with diphtheria toxin for eighteen hours, and of insulin previously mixed with diphtheria toxin and injected as soon as mixed (not incubated). Broken line represents the mean effect of five experiments using diphtheria toxin incubated with insulin for eighteen hours (table 10). Solid line represents the mean effect of five experiments, using diphtheria toxin mixed with insulin but not incubated (table 11).

Insulin not Affected by Diphtheria Toxin when Mixed Immediately before Injection.—The experiments show that when three minimum lethal doses of diphtheria toxin are mixed with one-fifth unit of insulin and injected immediately into a rabbit, the blood sugar curve coincides almost exactly with that in the control tests in which one-fifth unit was injected alone.

Insulin made Less Efficient when Incubated for Eighteen Hours at 37 C. with Diphtheria Toxin.—When one-fifth unit of insulin was incubated with three minimum lethal doses of diphtheria toxin for eighteen hours at 37 C. in a test tube, a change took place in the insulin. As the tables and chart reveal, when this mixture was injected into a rabbit, the insulin was less efficient than one-fifth unit of pure insulin in the control test. The blood sugar did not react as promptly, did not diminish as much and returned to normal sooner.

It can also be seen in the tables that one-fifth unit of pure insulin maintained its original efficiency even after it was incubated at 37 C. for eighteen hours. It is important that when the mixture of insulin and diphtheria toxin was injected, all the blood sugar curves were completed before any toxic signs appeared from the diphtheria toxin.

Apparently there are only two explanations as to the cause of the decreased efficiency of insulin in this experiment: One is that the insulin, when incubated in vitro, is actually rendered less efficient by some chemical phenomena. The other is, as Zeckwer and Mikami suggested, that the toxin has some immediate effect on the body cells, prior to the appearance of toxic symptoms, that inhibits the full action of insulin. They have shown that there is an immediate body reaction to injected toxin and the result is hyperglycemia.[26]

I believe their explanation to be true when large doses of toxin are injected. Small doses, however, seem to have little effect in producing hyperglycemia, but still affect insulin in vitro. I believe, therefore, that diphtheria toxin has a chemical action on insulin when they are incubated for eighteen hours at 37 C.

SUMMARY

1. There is a rise in the blood sugar level of rabbits, with the onset of symptoms of diphtheric intoxication.

2. A rise in the blood sugar level of rabbits is coincident with the onset of an allergic reaction.

3. The blood sugar level is slightly lowered during an intense malarial paroxysm in man.

4. A reduction in the action of insulin occurs during diphtheritic intoxication in rabbits.

5. The blood sugar level remains normal in rabbits following the injection of a mixture of three minimum lethal doses of diphtheria toxin and one-fifth unit of insulin, when injected fifteen minutes after they are combined.

6. Insulin becomes less efficient, as determined by the blood sugar level of rabbits, when incubated with diphtheria toxin for eighteen hours at 37 C.

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26. Zeckwer and Goodell (footnote 12). Mikami (footnote 20).

ROENTGEN TREATMENT OF ACUTE CERVICAL LYMPHADENITIS *

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Acute cervical lymphadenitis in children, secondary to infections of the upper respiratory tract, is frequently encountered, particularly in the locality about Newark. Many of the cases under observation proceeded to the stage of suppuration. Some radical deviation, therefore, from the usual course of treatment was considered. Attention was turned to the increasing number of reports in the current literature in which the treatment of patients who had various acute and chronic inflammations with roentgen rays was discussed favorably.

This type of treatment could also be expected to have a favorable effect on acutely inflamed lymphatic glands. Further justification for the application of roentgen therapy in cases of acute cervical lymphadenitis was the favorable experience of many German authors.

Until recently, the value of treating acutely inflamed tissue by the x-rays was not appreciated. Lawson,[1] in discussing this subject, emphasized the fact that too much attention was paid to malignant and allied conditions, to the utter neglect of some phases of radiology which would yield more satisfactory results. Much of the lack of enthusiasm for x-ray therapy at the present time is due to the poor results obtained when it was still in its infancy. The reasons for the early failures are obvious. At that time, the nature and the danger of handling x-rays were not known. Instruments were lacking for the accurate measurement of dosage, which today is considered highly important in the proper treatment of acutely inflamed tissue. Furthermore, results were not expected with the small doses that are now given. Experience taught that large doses aggravated acute infections; consequently, the conclusion was drawn that roentgenization was contraindicated in acute inflammatory conditions. Holzknecht,[2] in a consideration of the subject, predicted "a radical change in the therapy of acute and subacute coccus inflammations through the introduction of roentgen therapy."

As time elapsed, the interest of the medical profession was directed almost entirely to the possibilities of roentgen therapy in the treatment of persons who had malignant conditions. It was only in the field of

* Submitted for publication, Sept. 17, 1928.

1. Lawson, John D.: Treatment of Pyogenic Infection by Roentgen Irradiation, Radiology **6**:153 (Feb.) 1926.

2. Holzknecht, G.: Roentgen Treatment of Spontaneous, Post-Traumatic and Post-Operative Coccus Infections and Suppurations, Am. J. Roentgenol. **15**:332 (April) 1926.

dermatology that therapy by x-rays made progress and that its value was recognized in the treatment of superficial inflammations. Credit for the revival of the treatment of persons with acute and chronic inflammation by the roentgen rays belongs to Heidenhain and Fried.[3] In 1924, they reported their first series of cases, 243 in number, gathered over a period of a year and a half, and comprising about twenty different kinds of inflammatory conditions. In this series were included fifteen cases of cervical lymphadenitis in which good results were obtained in all but one instance. After the initial report of Heidenhain and Fried, x-ray therapy was used in almost every conceivable type of acute inflammation, most of the reports in the literature coming from German authors. In nearly every instance, the writer was enthusiastic, reporting favorable and gratifying results. Large series of cases have been reported by Heidenhain [4] alone, by Fried,[5] Lukowsky,[6] Schüler,[7] Bauer,[8] Kohler,[9] Kingreen,[10] Fraenkel and Nessnjewitsch [11] and others. Heidenhain and Fried had the most extensive experience. Of Heidenhain's series of 855 cases of acute inflammation of various kinds, 76 per cent showed quick and uneventful recovery. Seventy-five per cent of the 1,500 cases in Fried's series yielded good results.

The list of diseases for which these authors treated patients included arthritis, bursitis, carbuncle, epididymitis, erysipelas, furunculosis, gynecological inflammations, dental inflammations, lymphangitis, mastitis, orchitis, parotitis, peritonitis, paronychia and otitis media. Some authors limited themselves to the study of one disease. Kaess [12]

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3. Heidenhain, L., and Fried, C.: Röntgenbestrahlung und Entzündung, Arch. f. klin. Chir. **133**:64, 1924.

4. Heidenhain, L.: Roentgen Treatment and Inflammation, Strahlentherapie **24**:37, 1926.

5. Fried, C.: Die Röntgenbehandlung der akuten Entzündungen, Strahlentherapie **26**:484, 1927.

6. Lukowsky, A.: Zur Röntgenbehandlung von Entzündungen, Beitr. z. klin. Chir. **136**:554, 1926.

7. Schüler, R.: Ueber Röntgenbestrahlung akuter Entzündungen, München. med. Wchnschr. **73**:1580 (Sept. 17) 1926.

8. Bauer, F.: Roentgen Treatment of Inflammations, München. med. Wchnschr. **72**:646 (April 17) 1925; abstr. Am. J. Roentgenol. **15**:481, 1926.

9. Kohler, A.: X-Ray Treatment of Acute Suppurative Inflammations, Deutsche Ztschr. f. Chir. **203**:539, 1927.

10. Kingreen, O.: The Roentgen Irradiation of Acute Inflammations, Deutsche Ztschr. f. Chir. **197**:10, 1926; abstr. Am. J. Roentgenol. **17**:503 (April) 1927.

11. Fraenkel, S. R., and Nessnjewitsch, L. M.: Roentgen Treatment of Surgical Inflammatory Processes, Strahlentherapie **24**:87, 1926; abstr. Am. J. Roentgenol. **19**:190 (Feb.) 1928.

12. Kaess, F. W.: Ueber Röntgenbestrahlung bei postoperativer Pneumonia, Zentralbl. f. Chir. **52**:1084 (May 16) 1925.

treated ten patients with postoperative pneumonia, eight of whom promptly recovered. Platou, Schlutz and Collins [13] treated a series of patients with erysipelas by x-rays and compared them with a control group. In the irradiated group, the mortality was only 6 per cent, whereas in the control group it was 23 per cent. Levy and Golden [14] treated twenty patients with rheumatic carditis, seventeen of them showing definite improvement. These results seem to indicate that treatment for acute cervical lymphadenitis with x-rays is a rational therapeutic measure.

For two years, I had under my care eighty patients with acute cervical lymphadenitis who were treated by roentgen irradiation. All these cases occurred in children under 7 years of age, and the disease was secondary to infections of the upper respiratory tract. The cases included were not due to buccal infection, carious teeth, scalp infections, eczema, retropharyngeal abscess, tuberculosis of the glands or infectious mononucleosis. The inflammation occurred invariably in the superior deep cervical nodes. Moreover, all cases selected for this series were considered potentially suppurative, mild cases being excluded. No auxiliary treatment of any kind was used; reliance was placed on irradiation as the sole therapeutic measure. With the exception of two, all the patients were treated by Drs. Charles F. Baker and Ernst A. May of Newark.

Minimal doses were found essential. Heidenhain and Fried, in the beginning of their work, gave dosages consisting of over 20 per cent of the skin unit dose. Only when they reduced the amount to doses between 10 and 20 per cent, however, did they obtain good and consistent results. They found that higher doses would aggravate the inflammation and frustrate success. The average dosage given by Dr. May in these cases of acute cervical lymphadenitis was 20 per cent of one skin unit dose on the surface, with the use of from 150 to 180 kilovolts, ½ mm. zinc or copper plus 3 mm. aluminum filter and a focus skin distance of 30 cm. This dose is equivalent to 260 R units, one skin unit dose being equal to 1,300 R units ("R unit" means the international roentgen unit). The surface treated was always larger than the area of inflammation. As a rule, the younger the child or the more acute the inflammation, the smaller was the size of the dose given. When required, a second treatment was given after an interval of from five to seven days.

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13. Platou, E. S.; Schlutz, F. W., and Collins, L.: Erysipelas, Am. J. Dis. Child. **34**:1030 (Dec.) 1927.

14. Levy, R. C., and Golden, R.: Some Effects of Roentgen Irradiation of the Heart in Rheumatic Carditis, Am. J. Roentgenol. **18**:103 (Aug.) 1927.

RESULTS

Twelve patients developed suppuration; in the remaining sixty-eight patients (85 per cent), the inflammation subsided completely without surgical intervention. This result is better than that reported by most authors, probably due to the fact in most of the cases irradiation was performed early. Kohler [9] pointed out from his experience that results in regional cervical glands were very good, but that unfortunately most of the patients called for treatment when the nodes were already broken down. Schüler [7] believed that the reason for the variation in results obtained by the different observers would not be disclosed until the effect of radiation was fully explained. Lukowsky [6] suggested that possibly the patient's age and general condition were factors to be considered.

REPORT OF CASES

CASE 28.—Swelling of the nodes was discovered on March 2. On March 7, when the first treatment was given, there was a massive swelling of the nodes on the left side of the neck, which was very tender and painful to the touch. The periglandular tissues were red and edematous. There was an accompanying tonsillitis and catarrhal otitis media on both sides. The temperature was 104 F. Following irradiation, the temperature dropped gradually and the pain diminished. On March 12, the temperature was 101 F., but there was slight, if any, diminution in the size of the mass. It was, however, not so tender and painful, although still red and edematous. The ear drums were normal in appearance.

On March 14, a second treatment was given. On March 19, the swollen area was reduced to about one fourth its former size and all local signs of inflammation had subsided.

Comment.—Clinically, this was the type of case that frequently progresses to suppuration. Before the treatment was given, it seemed that this would be a good case to test. It was gratifying to note that, following the irradiation, the inflammation gradually subsided, and x-ray therapy appeared to favor resolution.

CASE 40.—On February 14, while the patient was in the fourth week of an attack of scarlet fever, a swelling of the nodes on both sides of the neck appeared. Both ears had been discharging for two days previously. On February 15, when both sides of the neck were irradiated, the temperature was 103.2 F. On February 21, the nodes were still large, but there were decidedly less heat and tenderness. The ears were still discharging profusely. Another treatment was given. On February 27, the swelling was about half its original size, and was only slightly tender. There was less discharge from the ears, and the temperature was only 100 F. On March 2 the ears had stopped draining, and on March 7 the mass had almost entirely disappeared. The patient had not received antitoxin.

Comment.—It is highly probable that this child would have recovered without x-ray treatment. The results secured, however, disproved the old theory that irradiation would aggravate the inflammation.

CASE 56.—This case is interesting in that the condition recurred. On both occasions, the inflammation of the nodes subsided following irradiation. The child developed a massive cervical adenitis with intense pain and tenderness. On April 6, four days after the enlargement was noticed, the swollen area was given an x-ray exposure. The temperature dropped to normal by April 8; two days later, the nodes receded to almost normal size. This was a rapid recovery. On April 25 there was a recurrence, with an almost identical picture. On April 29 the region was irradiated, and again there was the same rapid disappearance of the mass.

CASE 71.—This patient had two previous attacks of acute cervical lymphadenitis; each time there was suppuration. When the adenitis developed for the third time, it was expected that still another incision would have to be made.

On April 28, only two days after the mass was first noticed, the area was irradiated, a dose of 260 R units being given. By April 29, the temperature had dropped to normal and all signs of inflammation had disappeared. On May 2, the nodes were reduced nearly to their normal size.

CASE 46.—On January 6, a large mass in the neck was discovered. When the patient was given an exposure on January 8, the nodes on the right side were tremendously enlarged. There was severe pain on motion. The area was very hot and tender. The temperature at the time was 104 F. On January 11, the fever had disappeared; two days later, the nodes were scarcely palpable.

Comment.—This case occurred in a child with a congenital malformation of the heart. Since birth, because of the cardiac defect, any infection that developed had been treated most energetically. For this reason, irradiation was employed. It was gratifying to see a rapid recovery.

CASE 37.—In this typical suppurative case, a mass in the neck was first noticed on June 2. The child was examined on June 7. The temperature at the time was 104 F. The nodes on the right side of the neck were tremendously enlarged, with marked local heat, tenderness and much pain. The periglandular tissues were red and edematous.

The area was treated with the roentgen rays on the day of examination. By June 11, there was definite fluctuation. When a small pricking incision was made into the area, about 30 cc. of watery pus escaped; a drain was introduced and retained until June 13. Two days later the wound was healed, with very little induration of underlying structures. The cosmetic result was excellent.

Comment.—The case clearly brings out the following points: 1. Roentgen irradiation will accelerate the process of suppuration. 2. Tiny incisions are sufficient for ultimate healing. 3. A better cosmetic effect is obtained with irradiation.

COMMENT

Every patient with acute cervical lymphadenitis and a high temperature should be treated by roentgen irradiation, for by this method there is everything to be gained and nothing to be lost. An unfavorable effect from such treatment is not reported in any case. From the standpoint of scientific therapy, little advance has been made in the treatment

Table Showing Effect of Roentgen Irradiation on Eighty Cases of Acute Cervical Lymphadenitis

Case	Age	Sex	Approximate Duration of Enlargement of Nodes Before Irradiation, Days	Other Symptoms and Associated Conditions at Time of Irradiation	Number of Treatments	Tonsils Present or Absent	Result
1	8 mo.	F	4	Rhinopharyngitis, tonsillitis, pyelitis; 103.2 F.	1	+	Resolution in about 8 days
2	2 yr. 1 mo.	F	6	Rhinopharyngitis, tonsillitis, bilateral purulent otitis media, acute tracheobronchitis; 103.6 F.	1	+	Resolution in about 10 days; ear infection subsided in about 5 days
3	1 yr. 2 mo.	M	2	Tonsillitis, bilateral catarrhal otitis media, rhinitis; 104.2 F. ..	1	+	Resolution in about 6 days; ear infection subsided in about 5 days
4	7 mo.	F	8	Bilateral involvement of nodes, extremely tender, painful and swollen; 103.4 F.	1	+	Resolution in about 12 days; fever persisted for 5 days
5	8 mo.	M	3	Severe infection of upper respiratory tract; rhinopharyngitis, catarrhal otitis, tonsillitis, bilateral involvement of nodes; marked embarrassment to respiration; 103.2 F.	1	+	Resolution in about 10 days
6	3 yr. 2 mo.	F	11	No symptoms other than enlarged nodes, unilateral swelling with periglandular infiltration; 102 F.	1	—	Resolution in about 20 days
7	11 mo.	M	2	Rhinopharyngitis, tonsillitis, unilateral involvement of nodes; child toxic; 104 F.	1	+	Resolution in about 18 days
8	3 yr. 1 mo.	F	6	Unilateral involvement accompanied by extreme pain and tenderness; 102.8 F.	1	+	Resolution in about 18 days
9	7 yr.	M	12	No symptoms other than swollen, painful and tender nodes on right side only; 101.6 F.	2	—	Resolution in about 16 days
10	1 yr. 4 mo.	M	4	Tonsillitis, rhinopharyngitis, purulent otitis, tremendous swelling of nodes on both sides; prostration; 103.2 F.	1	+	Resolution of nodes in about 8 days; ear infection cleared up in 11 days
11	3 yr. 11 mo.	M	6	Tonsillitis, laryngitis, massive swelling on both sides of nodes, occurring in patient with celiac disease; 102.4 F.	1	—	Resolution in about 26 days
12	5 yr. 6 mo.	F	8	No symptoms to account for fever other than unilateral swelling of nodes; 103 F.	1	—	Resolution in about 6 days
13	1 yr. 2 mo.	F	4	Bilateral purulent otitis media, tonsillitis, bilateral adenitis, accompanied by great pain, heat and swelling of the nodes on both sides; 104.2 F.	1	+	Resolution in about 12 days; ear infection cleared up in 8 days
14	1 yr. 11 mo.	M	4	Unilateral massive enlargement of nodes, painful, extremely tender and swollen; hot to touch; suppurative gland on opposite side three months previous; 104.4 F.	1	+	Resolution in 6 days; temperature normal in 5 days
15	1 yr. 7 mo.	M	3	Rickets, tonsillitis, rhinopharyngitis, unilateral involvement of nodes; 103 F.	1	+	Resolution in about 19 days
16	4 yr. 6 mo.	F	5	Rhinopharyngitis, tonsillitis, unilateral catarrhal otitis; nodes on both sides hot, tender and massively swollen; 104.2 F.	1	+	Resolution in about 17 days
17	10 mo.	M	4	Nodes becoming larger each day; extremely tender, hot and swollen, more marked on right side; 103.4 F.	1	+	Resolution in 9 days

18	3 yr. 2 mo.	F	8	Bilateral otitis, pyelitis, marked tender, swollen nodes; 102.4 F.	1	+	Resolution in about 13 days
19	11 mo.	M	5	Bilateral purulent otitis media, rhinopharyngitis, tonsillitis; unilateral involvement of nodes; 104 F.	1	+	Resolution in about 4 days
20	3 yr. 7 mo.	M	8	Massive enlargement of right side only, with great pain and tenderness; 102.8 F.	1	+	Resolution in about 28 days
21	2 yr. 11 mo.	F	7	Tremendous enlargement of nodes on right side, with periglandular infiltration, redness, swelling and heat; 104 F.	1	—	Suppuration; fluctuation evident 3 days following x-ray exposure
22	3 yr. 1 mo.	F	5	Unilateral severe infection of nodes; large, tender and painful; 103.6 F.	1	—	Nodes receded in about 12 days; fever persisted 6 days
23	1 yr. 6 mo.	M	9	Malnutrition, tonsillitis, bilateral involvement; right side affected more than left; 102 F.	2	+	Suppuration
24	1 yr. 8 mo.	M	8	Tremendous swelling of nodes, with heat; tenderness and pain on motion; unilateral involvement; 102.2 F.	1	—	Resolution in about 21 days
25	3 yr.	F	3	Unilateral involvement; rhinopharyngitis; toxic; 104.2 F.	1	—	Resolution in about 12 days
26	1 yr.	M	3	Rhinopharyngitis, tonsillitis, unilateral involvement, accompanied by marked redness and edema of periglandular tissues; 104 F.	1	+	Resolution in 6 days
27	1 yr. 9 mo.	F	8	Bilateral involvement of nodes, more marked on left side; rhinopharyngitis, severe tonsillitis, tracheobronchitis; 103.4 F.	1	+	Resolution in 11 days
28	2 yr. 6 mo.	M	5	Bilateral catarrhal otitis media, tonsillitis, rhinopharyngitis; massive swelling of nodes on left side with much heat, tenderness and pain; 104 F.	2	+	Resolution in 14 days
29	7 mo.	M	6	Rhinopharyngitis, tonsillitis, unilateral purulent otitis media; 102.6 F.	1	+	Resolution in 9 days; ear infection subsided in 12 days
30	2 yr. 2 mo.	F	2	Tonsillitis; nodes on left side tremendously swollen; local heat, tenderness and pain; 103.8 F.	2	+	Resolution in 26 days
31	1 yr. 3 mo.	M	11	Congenital syphilis; unilateral swelling of nodes; 103.3 F.	1	+	Suppuration
32	5 yr. 6 mo.	M	14	No symptoms or signs other than massive, unilateral enlargement of the nodes to account for fever; 101.4 F.	2	—	Resolution in 28 days
33	1 yr. 1 mo.	F	2	Severe infection of nodes, left more than right; tremendously swollen; extremely tender and painful; toxic; 104.2 F.	1	+	Resolution in 8 days; temperature returned to normal in 4 days
34	3 yr. 2 mo.	M	7	Pharyngitis; nodes on right side involved; malnutrition; 103.6 F.	1	—	Resolution in about 19 days
35	1 yr. 11 mo.	F	9	Rhinopharyngitis; massive swelling of nodes on left side; 102.2 F.	1	+	Resolution in 5 days
36	2 yr. 7 mo.	F	5	Pharyngitis, bilateral swelling of nodes, tracheobronchitis; malnutrition; 103.6 F.	1	+	Resolution in 18 days
37	3 yr.	M	5	Pharyngitis, tremendous swelling of nodes on right side, with marked redness, heat and tenderness; pain on touch and motion; 104 F.	1	—	Rapid suppuration; pricking incision 4 days after irradiation
38	11 mo.	F	4	Rhinopharyngitis; bilateral involvement of nodes; periglandular redness and edema; marked local pain and tenderness; 104 F.	1	+	Resolution in about 8 days
39	8 mo.	F	8	Rickets; bilateral catarrhal otitis media; left-sided involvement of nodes; marked redness, swelling and much heat; 102.6 F.	1	+	Suppuration evident in about 4 days after irradiation
40	4 yr. 6 mo.	M	3	Purulent otitis media; marked subjective pain in nodes on both sides occurring in fourth week of scarlet fever; 103.2 F.	2	—	Resolution in about 20 days; ears ceased discharging in 9 days

Table Showing Effect of Roentgen Irradiation on Eighty Cases of Acute Cervical Lymphadenitis—Continued

Case	Age	Sex	Approximate Duration of Enlargement of Nodes Before Irradiation, Days	Other Symptoms and Associated Conditions at Time of Irradiation	Number of Treatments	Tonsils Present or Absent	Result
41	6 yr. 8 mo.	M	10	Nodes on one side gradually becoming larger each day; bilateral purulent otitis; rhinitis; 102 F.	1	—	Resolution in about 20 days; ears cleared up in about 16 days
42	2 yr.	M	6	Recovering from measles; both sides involved, right much more than left; acutely inflamed, with a great deal of discomfort; 103 F.	2	+	Resolution in about 17 days
43	2 yr.9 mo.	F	10	Developed large acutely inflamed nodes immediately after tonsillectomy, unilateral; marked pain and tenderness; 102.2 F.	2	—	Suppuration; fluctuation evident in about 9 days after first irradiation
44	1 yr. 3 mo.	F	5	Rhinitis, tonsillitis; tremendous swelling of nodes on right side; redness, local heat and pain; 103.4 F.	1	+	Rapid resolution; nodes subsided in about 5 days
45	3 yr. 1 mo.	M	8	Tonsillitis; tremendously swollen nodes on both sides; pyelitis; 104 F.	2	+	Resolution in about 13 days
46	6 yr. 10 mo.	M	2	Congenital malformation of heart; tonsillitis; 104 F.	1	+	Resolution in 6 days
47	11 mo.	F	6	Massive enlargement of nodes on both sides; severe tonsillitis; difficulty in breathing; 103.8 F.	1	+	Resolution in about 9 days
48	5 yr.	F	8	Unilateral nodes acutely inflamed, very red, swollen, with local heat and tenderness; 102 F.	1	—	Resolution in about 16 days
49	11 mo.	M	4	Rhinopharyngitis, tonsillitis; bilateral involvement of nodes; both sides equally inflamed; 104.4 F.	1	+	Resolution in about 6 days
50	6 yr.	F	8	Unilateral involvement accompanied by marked subjective distress; 102.2 F.	2	—	Resolution in about 21 days
51	4 yr. 2 mo.	M	16	Bilateral swelling of nodes; very tender and hot to touch; 101 F.	3	—	Resolution in about 2 months
52	4 yr. 6 mo.	M	9	Tonsillitis; unilateral involvement; marked periglandular redness and edema; much heat and tenderness; 104 F.	1	+	Suppuration evident in 3 days after irradiation; rapid healing after pricking incision
53	1 yr. 7 mo.	F	4	Rhinopharyngitis, severe tonsillitis; huge swelling of nodes on right side, with much local heat and tenderness; 103.6 F.	1	+	Resolution in about 11 days
54	6 mo.	F	2	Tonsillitis; tremendous swelling of nodes on both sides; 104.2 F.	1	+	Resolution in about 7 days
55	4 yr. 6 mo.	F	10	No apparent cause for temperature other than enlarged nodes; unilateral involvement; extremely tender and painful; 101.4 F.	1	+	Resolution in about 18 days
56	2 yr. 9 mo.	F	4	Tonsillitis; unilateral involvement; recurrent case; 103.8 F.	2	+	Resolution in 8 days
57	9 mo.	M	3	Severe infection of upper respiratory tract; rhinopharyngitis, tonsillitis, bilateral catarrhal otitis media; tremendous swelling of nodes on right side; 103.2 F.	1	+	Resolution in about 9 days
58	2 yr. 1 mo.	M	5	Massive swelling of nodes on both sides of neck; tonsillitis, rhinopharyngitis, tracheobronchitis; 103.8 F.	2	+	Suppuration on about the 12th day
59	9 mo.	F	3	Rhinopharyngitis, conjunctivitis, tonsillitis; bilateral involvement; malnutrition; 105 F.	1	+	Resolution in about 9 days
60	20 mo.	M	4	Rhinopharyngitis, tonsillitis; left purulent otitis media; massively swollen nodes on left side; 103.2 F.	1	+	Resolution in about 8 days

61	3 yr. 1 mo.	F	7	Bilateral involvement of nodes, with marked redness, local heat and periglandular edema on both sides; 103.2 F.	2	—	Resolution in about 40 days
62	6 yr. 8 mo.	F	12	Huge swelling of nodes on right side; extremely sensitive to touch; local redness, swelling and heat; periglandular edema; 101 F.	2	+	Resolution in about 22 days
63	1 yr. 1 mo.	M	4	Rhinopharyngitis, tonsillitis; unilateral involvement; rickets; 102.2 F.	1	+	Resolution in about 17 days
64	4 yr.	M	6	Developed enlarged nodes on left side about three days after tonsillectomy; much local heat, redness, pain and tenderness; periglandular tissues hard and infiltrated; 104 F.	1	—	Suppuration 4 days following exposure
65	1 yr. 2 mo.	M	5	Tonsillitis, bilateral catarrhal otitis media; bilateral involvement of nodes; both sides very swollen, tender and painful; 104 F.	1	+	Resolution in about 17 days
66	2 yr. 2 mo.	F	6	Tonsillitis, rhinopharyngitis; nodes on left side involved; very hot and tender to touch; pyelitis; 103.6 F.	2	+	Resolution in about 12 days
67	3 yr. 9 mo.	F	5	Rhinopharyngitis; left catarrhal otitis media; unilateral involvement of nodes; 104.2 F.	1	—	Resolution in about 5 days; ear infection subsided in 3 days
68	3 yr. 2 mo.	F	8	Tremendous swelling of nodes on left side, with brawny periglandular infiltration; 102 F.	1	—	Suppuration evident about 4 days after irradiation
69	4 yr. 9 mo.	M	8	Marked discharge from both ears; massive swelling on right side with extreme pain, tenderness and heat; 103.8 F.	1	—	Resolution in about 28 days; ear infection cleared up in 11 days
70	8 mo.	M	5	Unilateral involvement of nodes; severe tonsillitis, tracheobronchitis; 104 F.	2	+	Suppuration evident on about 14th day after irradiation
71	6 yr.	M	2	Tenderness, pain and extreme heat over mass; much discomfort; 102.2 F.	1	—	Resolution in about 7 days
72	1 yr. 2 mo.	F	8	Rhinopharyngitis, tonsillitis; bilateral purulent otitis media; bilateral swelling; 104 F.	2	+	Resolution in about 20 days; ear infection cleared up in 10 days
73	1 yr. 8 mo.	F	5	Tonsillitis, rhinitis, tracheobronchitis; nodes on right side tremendously swollen, accompanied by extreme local heat, pain and tenderness; 103.2 F.	1	+	Resolution in about 6 days
74	6 yr.	M	7	Unilateral swelling of nodes; marked redness, tenderness and heat; pain on rotating head; 102.2 F.	2	+	Resolution in about 18 days
75	11 mo.	F	5	Catarrhal otitis media; bilateral involvement of nodes; tonsillitis, rhinopharyngitis; 104 F.	1	+	Resolution in about 5 days
76	4 yr. 11 mo.	M	8	Massive swelling of nodes on right side; rhinopharyngitis; 102.4 F.	3	+	Resolution in about 2 months
77	2 yr. 6 mo.	M	6	Rhinopharyngitis, tonsillitis; bilateral involvement, right more inflamed than left; toxic; 104 F.	1	+	Resolution in about 20 days; temperature normal in about 7 days
78	11 mo.	M	5	Toxic; bilateral purulent otitis media; massively swollen, tender nodes; severe tonsillitis; difficulty in breathing; 103.6 F.	1	+	Resolution in about 15 days; ears ceased discharging in 8 days
79	3 yr. 2 mo.	M	10	No other symptoms than fever, swelling and tenderness of nodes on right side; 102 F.	2	—	Suppuration evident in about 12 days
80	2 yr. 9 mo.	F	5	Tonsillitis, rhinopharyngitis; unilateral catarrhal otitis media; 104.2 F.	1	+	Resolution in 9 days

of acute cervical lymphadenitis. Epstein,[15] for example, stated that the usual treatment was the application of ichthyol ointment, used almost like a specific, without sufficient therapeutic reason. On the other hand, x-rays are an agent with known penetrative powers and a remedy proved by histologic studies to exert a favorable effect on inflamed tissue.

Cases 46 and 49 illustrate rapid recovery following irradiation. As a general rule, if the patient receives treatment by the third or fourth day, the inflammation will subside; each day that irradiation is deferred lessens the chance of recovery without suppuration.

Cases 37 and 68 show that the application of roentgen rays will hasten the process of suppuration and recovery. In patients not treated by the roentgen rays, from two to three weeks are required to break down the mass and often as many weeks to heal it. However, in most of the conditions for which irradiation was employed and in which it was necessary to make an incision, healing occurred in about ten days. The same course of events seems to hold true for other inflammatory conditions. Lawson,[1] who studied the effects of irradiation on pyogenic infections in general, made the definite statement that x-ray treatment will shorten the length of time the lesion is present and active. Fried,[5] too, observed that the duration of acute inflammatory conditions is shortened by roentgen therapy.

Sixteen of the eighty cases were complicated by an acute otitis media, but mastoiditis did not develop.

Heidenhain and Fried stated that the process of lymphadenitis in general is accelerated by irradiation. There is either a rapid retrogression of the inflammatory area or a rapid breakdown. If suppuration develops, the redness of the surrounding region decreases and the swelling recedes quickly, becoming localized as a small soft area which may be evacuated by a slight pricking incision. An advantage of the new method of treatment, they affirmed, is that the course of the disease is much shortened and, if the case goes on to suppuration, the need for surgical intervention is reduced to a minimum. The result of irradiation is far better from a cosmetic standpoint than in patients operated on and not treated by irradiation. All observers note that x-ray treatment not only accelerates the local inflammatory process, but relieves pain and discomfort. An improvement in the constitutional symptoms takes place, and in most cases there is a decided drop in temperature in about forty-eight hours. The analgesic effects of x-rays

15. Epstein, J.: The Therapeutics of Some of the Common Ailments in Children, Arch. Pediat. **45**:339 (June) 1928.

are well discussed in an article by Albert.[16] From a clinical point of view, the use of irradiation is particularly desirable in young infants; they seem to suffer most, and in them the results are more striking than in older children.

ACTION OF X-RAYS

The action of x-rays on inflamed tissues has not been explained definitely. It is known, however, that they do not kill bacteria, at least not in the dosage to which the human body can be exposed. As a result of his laboratory experiments, Fried [5] stated that roentgen rays caused an increase in the bactericidal power of the blood serum recognizable from twelve to twenty-four hours after irradiation, and reaching its highest point in from twenty-four to forty-eight hours and disappearing again after from six to eight days. Fraenkel and Nessnjewitsch [11] could not find any increase in the bactericidal power of the blood serum, and they believe that the effect of x-rays is purely local. Pordes' [17] theory, which is quite popular, is that the leukocytes are very sensitive to x-rays; when the inflamed area is irradiated, even with small doses, the white blood cells break down and the bacteriolysins and antitoxins become released and effective.

Motojima [18] made an extensive and thorough study of the action of x-rays on acutely inflamed tissues. Histologically, he was able to demonstrate clearly the favorable influence of roentgen irradiation on local inflammation. By setting up chemical and bacterial irritation in the tissues of rabbits, he showed by microscopic examination that x-rays caused a decrease in the infiltration of inflammation around the site of the irritant. He stated that the x-rays had both general and local effects. The general effect was a nonspecific stimulation of the immunizing power of the body. Locally, they caused a dilatation of the blood vessels and a hyperemia with a resultant increase in the flow of blood and lymph, thereby bringing the natural defensive powers of the body to the inflamed area. At an earlier date, May and Holfelder [19] also determined from histologic studies that, after irradiation, active hyperemia occurs around the focus of infection, together with an increased circulation of the lymph.

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16. Albert, S.: X-Rays in the Treatment of Various Inflammatory Conditions, Rhode Island M. J. **80**:90 (June) 1925.

17. Pordes, F.: Prinzipielle Fragen der biologische Röntgenstrahlenwirkung, Jahresk. f. ärztl. Fortbild. **14**:23 (Aug.) 1923.

18. Motojima, R.: Experimental Investigations on the Influence of X-Rays on the Course of Inflammatory Processes and Their Comparison with Other Physical Methods, Strahlentherapie **29**:30, 1928.

19. May, E. A., and Holfelder, H.: Die Röntgenbehandlung der nicht tuberculosen Knochen und Gelenkerkrankungen, in Salzmann, F.: Roentgenbehandlung innerer Krankheiten, Munich, Lehmanns, 1923, p. 117.

SUMMARY

Roentgen therapy has been used with good results in a variety of acute infections as histologic evidence has demonstrated. It use is warranted, therefore, in the treatment of acute cervical lymphadenitis.

Eighty patients were treated; sixty-eight recovered without suppuration.

Acute cervical lymphadenitis is almost always of prolonged duration. Roentgenization accelerates the inflammatory process, so that there is either rapid resolution or rapid breaking down.

Following the exposure, there is relief of pain and discomfort, and improvement in the constitutional symptoms.

Unfavorable effects do not result from irradiation.

Roentgen therapy, although it reduces the need for surgical intervention to a minimum, cannot supplant it.

CONCLUSION

Roentgen irradiation for acute cervical lymphadenitis is the most successful treatment for this condition. The earlier the treatment is given, the better the result.

THE BACTERIOLOGY OF MASTOIDITIS IN INFANTS*

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Ever since Hartmann,[1] in 1898, followed by Preysing [2] in 1904, noted in infants digestive disturbance associated with disease of the middle ear, the rôle of parenteral infection in gastro-intestinal disturbance has been under consideration.

In 1921, Maurice Renaud,[3] in seventy autopsies in cases of diarrhea, found suppuration of the middle ear and mastoid in every case, but did not discover any pathologic condition of the gastro-intestinal tract. Floyd,[4] in 1925, reported twenty-six cases, occurring within eighteen months, with symptoms of gastro-intestinal disturbance, toxicity and loss of weight, in infants from 8 to 15 months of age. The earlier cases did not show any response to medical treatment, and autopsy revealed only pus, too thick to flow, in the mastoids. Mastoidectomy in such cases gave good results.

At the St. Louis Children's Hospital, similar cases have been studied in an effort to correlate the clinical observations with the organisms found in cultures. Alden [5] reported that in thirty-five cases of subperiosteal abscess (mastoid) occurring in the course of six years, the majority of the cultures made showed staphylococci or nonhemolytic streptococci. On the other hand, cultures from the ears of thirty-two infants with the other form of mastoiditis (i.e., with constitutional rather than local signs) almost without exception showed hemolytic streptococci. This suggested bacterial specificity in each form of the disease.

Alden and Lyman [6] reported fifteen cases in infants from 2 to 14 months old in which mastoidectomy was performed because of nutritional

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* Submitted for publication, Aug. 1, 1928.

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1. Hartmann: Die Einwirkung der Otitis Media der Säuglinge auf den Verdaungsapparat, Eintschr. f. Ohrenh. **34**:1, 1898.

2. Preysing: Otitis Media der Säuglinge, Wiesbaden, J. F. Bergmann, 1904.

3. Renaud, Maurice: Bull. et mém. Soc. méd. d. hôp de Paris **44**:1326, 1352 and 1384, 1921.

4. Floyd: Masked Mastoiditis Simulating Alimentary Intoxication, Arch. Otolaryng. **1**:411 (April) 1925.

5. Alden, Arthur M.: Mastoid Infections in Infants, Arch. Otolaryng. **5**:39 (Jan.) 1927.

6. Lyman, H. W., and Alden, A. M.: Gastro-Intestinal Disturbances in Infants as the Result of Obscure Infection of Mastoids, Laryngoscope **35**:586 (Aug.) 1925.

disturbance. Eleven cases showed hemolytic streptococci in the culture; one showed pneumococci, and three cultures were lost. Marriott [7] concluded that the symptom complex (prostration, emaciation, diarrhea, vomiting and acidosis) is probably a specific intoxication, since it does not appear in other equally high fevers or in mastoiditis due to other organisms such as pneumococci.

In an effort to corroborate these observations, a bacteriologic study was made of the disease of the mastoid and middle ear, at the St. Louis Children's Hospital, from October, 1926, to May, 1927. During this period, sixty-one patients were operated on, and in forty-three cases a double mastoidectomy was performed; altogether, therefore, cultures were made from 104 mastoids. In sixty-nine of 101 cases in which cultures were made from the ear, they were from both ears, giving a total of 170 cultures.

Unfortunately, although every patient who was operated on had paracentesis performed at least once, only twenty-five had had cultures taken from the ear; fifteen of these had had cultures made from both ears. Thus, forty cultures from the ear were followed by cultures from the mastoid.

The cultures made from the mastoid were immediately placed on blood agar plates. The cultures from the ear were made in one of two ways: Either the paracentesis knife, immediately after myringotomy, was inoculated on a blood agar slant; or this knife was wiped on a sterile swab wet in broth, and with this swab, an inoculation was made on a blood agar plate. In every case but eight, culture was made from material obtained at the first paracentesis.

Eighteen of the sixty-one operations on the mastoid were performed on older children, from 2 to 10 years of age. In all these cases, the indications for operation were frankly surgical. Of the infants under 14 months of age, eight were operated on because of localized indications, six for subperiosteal abscess and two for chronic otitis media.

The remaining thirty-seven patients were operated on for a complex of symptoms which were chiefly constitutional. These were patients with disease of the middle ear who showed, after repeated paracentesis, a continuation of fever, and loss of weight or failure to gain. Twenty-five had diarrhea and eleven vomiting. While in these cases there was no evidence of swelling over the mastoid, there was usually a sag of the posterior superior canal wall.

Considering that the indications in these cases were mainly medical, it may be significant that in only one case were the cultures from both

7. Marriott, McKim: Observations Concerning the Nature of Nutritional Disturbances, read before the American Pediatric Society, Washington, D. C., May 5, 1925.

mastoids sterile. In four other cases the culture from one mastoid was sterile, while that from the other showed a growth. This may be explained by the custom, if the otitis is bilateral, of performing a double antrotomy, in the absence of contraindications.

The occurrence of the different types of bacteria is noted in table 1. Many of the cultures showed two or more organisms. Thirteen of the 104 cultures from mastoids showed a mixed growth, and eighty-two showed a pure growth of a single organism (nine cultures were sterile). On the other hand, eighty-three or nearly half of the 170 ear cultures showed two or more organisms. All the mastoid cultures, moreover, were taken at the original operation, and all but eight of the 170 ear cultures were planted by the paracentesis knife that first opened the ear drum. The results of these cultures appear in table 1.

TABLE 1.—*Cultures from Middle Ears and from Mastoids*

Mastoid				Ear		
Total	In Pure Culture	Strain Hemolytic	Name of Organism	Total	In Pure Culture	Strain Hemolytic
32	22	13	Staphylococcus	141	61	16
34	33	34	Streptococcus hemolyticus	8	1	8
1	1	..	Nonhemolytic streptococcus	3	..	..
3	1	..	Streptococcus viridans	4	2	..
15	14	..	Pneumococcus	5	1	..
11	3	..	Diphtheroid	48	8	..
6	3	4	Bacillus coli	8	..	2
2	2	2	Bacillus of Morgan	4	..	4
1	1	..	Bacillus proteus	2	..	..
1	..	..	Micrococcus catarrhalis	..	..	..
..	..	..	Bacillus influenzae	1	..	..
..	..	..	Trichomycetes*	13	1	..
1	1	..	Bacillus pyocaneus	3	1	..
1	1	..	Bacillus of subtilis group	14	..	..
9	..	..	No growth	5	..	..

* In no case did these higher bacteria appear in less than two days after the culture was planted; usually not until three or four days after.

It is interesting to compare the figures in table 1 with those of Smith.[8] Of the fifty cases of cultures from the ear which he reported, many were made from one to three weeks after the ears began to drain; yet only twelve showed a mixed growth.

Ersner[9] reported that 63 per cent of the organisms found in the mastoid wound were the same as those found in cultures obtained from the external auditory canal; in one third of the cases they did not coincide, and 9 per cent of the cultures were sterile.

In my cases, forty cultures made from the ear were followed by operation and by a culture made from the corresponding mastoid. In only thirteen cases was the same organism found in the ears and mas-

8. Smith, D. T.: Causes and Treatment of Otitis Media, Am. J. Dis. Child. **28**:1 (July) 1924.

9. Ersner, M. S.: Bacteriological Analysis of Acute Mastoid Disease; Analytical Report of Mastoid Operations, Atlantic M. J. **28**:578 (June) 1925.

toids. In seven of these thirteen cases, the organism found alone in the mastoid was one of two or more found in the culture from the ear; in two cases the organism found in pure culture in the ear was found mixed with other organisms in the mastoid; in one case the same mixture of two organisms, and in another the same mixture of three organisms, was found in both ear and mastoid. Among forty cultures there was but one in which the same organism was found in pure culture in both ear and mastoid.

Of the eight infants with local symptoms in the mastoid, five showed hemolytic streptococci; one case, hemolytic streptococci on one side, and

TABLE 2.—*Organisms Found in Cultures Made from Older Children*

Name of Organism	Number of Cases
Hemolytic streptococcus (pure culture)	7
Hemolytic streptococcus on one side, hemolytic staphylococcus on the other	1
Streptococcus viridans on both sides (mixed with staphylococcus on one side)	1
Pneumococcus (pure culture)	1
Pneumococcus and staphylococcus	1
Hemolytic staphylococcus	3
Nonhemolytic staphylococcus and diphtheroid on one side; hemolytic staphylococcus and diphtheroid and streptothrix on other side	1
B. pyocaneus	1
B. proteus	1
No growth	1

TABLE 3.—*Organisms Found in Cultures Made from Infants with Severe Diarrhea*

Name of Organism	Number of Cases
Pneumococcus (pure culture)	4
Pneumococcus on one side, with B. coli on the other	2
B. coli alone (communior)	1
B. coli mixed with staphylococcus	2
B. coli mixed with B. subtilis	1
Bacillus of Morgan	1
Streptococcus hemolyticus	6
Staphylococcus hemolyticus	4
Staphylococcus, nonhemolytic	2
No growth	1
Cultures incomplete	1

pneumococci type IV on the other side; one case, pneumococci alone, and one case, staphylococci on both sides.

In the group of eighteen cases among older children, whenever the staphylococcus appeared alone, it was a hemolytic strain; in the mixed cultures a nonhemolytic strain was found (table 2).

Of the thirty-five infants operated on for "medical indications," twenty-five had severe diarrhea. Table 3 shows the results obtained on culture.

In every instance in which *B. coli* was cultured from the mastoids, diarrhea was the prominent symptom; the same was true of the one case from which the bacillus of Morgan was isolated. Only 60 per cent of the patients with pneumococci and 25 per cent of those with streptococci or staphylococci suffered from diarrhea.[10]

10. A case showing two organisms is used in calculating the percentage of both.

Among the sixty-one cases, there were thirteen deaths. Four of the deaths occurred in children from 2½ to 6 years of age: of these, two showed hemolytic streptococci; one, pneumococci type III, and one, no growth.

One child, aged 6 months, died after an operation for subperiosteal abscess with *Streptococcus hemolyticus* on culture. He died twenty-seven days after mastoidectomy, from causes unrelated to his mastoiditis.

The remaining eight deaths in infants were in patients operated on for constitutional symptoms (in the presence of otitis media). Loss of weight and diarrhea occurred in every case, and vomiting in half the cases. The results of cultures are noted in table 5.

TABLE 4.—*Organisms Found in Cultures Made from Eleven Patients in Whom Vomiting Was a Symptom*

Name of Organism	Number of Cases
B. coli alone	1
B. coli with staphylococcus	1
B. coli with pneumococcus	1
Bacillus of Morgan	1
Streptococcus hemolyticus	4
Staphylococcus nonhemolyticus	3
Staphylococcus hemolyticus	2

TABLE 5.—*Organisms Found in Cultures Made from Infants Showing Constitutional Symptoms*

Name of Organism	Number of Cases
Staphylococcus hemolyticus	2
Staphylococcus nonhemolyticus	2
Bacillus of Morgan	1
Pneumococcus, type 1	1
Pneumococcus, type 2, in one side; B. coli, nonhemolytic staphylococcus and diphtheroid in the other side	1
Incomplete culture	1

CONCLUSIONS

1. Cultures from the middle ear of infants are valueless as indications of the causative organism of an accompanying mastoiditis.

2. Infants suffering from otitis media and showing the constitutional symptoms of vomiting, diarrhea and failure to gain in weight often have infected mastoid antrums.

3. In all cases in which intestinal organisms (*B. coli-communior* or bacillus of Morgan) were found on culture from the mastoids, the prominent clinical symptom was diarrhea, accompanied in some instances by vomiting.

4. Pneumococci, streptococci and staphylococci were also found frequently in cultures from the mastoids of infants. These organisms did not give rise to a characteristic symptomatology.

THE WATER CONTENT OF BLOOD SERUM

A COMPARISON OF THE DETERMINATION OF THE SPECIFIC GRAVITY BY THE FALLING DROP METHOD AND BY SEVERAL OTHER METHODS *

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Dehydration of the blood plasma and interstitial body fluids is the outstanding bodily change caused by severe diarrheal disease in infants. The initial therapeutic indication is usually an energetic attempt to repair this condition by the administration of fluids. It is obvious that a convenient and dependable method of determining the degree of dehydration and the effect of therapeutic measures would be useful clinically. Measurement of change in the water content of the blood plasma would seem to be the most practicable index of dehydration. The blood plasma should exhibit a wider range of change in water content than whole blood for the reason that the circumstances producing dehydration cause a much more extensive withdrawal of water from the plasma than from the red cells.

A number of rather time-consuming gravimetric procedures have been suggested for the purpose of ascertaining the degree of dehydration. Thus, the specific gravity of the plasma may be obtained by weighing a measured volume of plasma, and the water content determined by weighing the residue from a measured volume of plasma after desiccation. Since protein constitutes more than 90 per cent of the total solids of the plasma, variation in the concentration of this substance is commonly used as an index of change of water content, as may be estimated by refractometric analysis of the plasma protein. As only a small sample, a drop or two, is required for this measurement, it is regrettable that this method, so suitable for clinical use, has not a sharper accuracy.

Most desirable from the point of view of clinical practicability and of probably sufficient accuracy is the falling drop method for determining specific gravity; this technic was recently devised by Barbour and Hamilton,[1] who found it possible to calculate density with an accuracy of 1×10^{-4}. The principle of this method involves the timing of the fall

* Submitted for publication, Aug. 24, 1928.

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1. Barbour, H. G., and Hamilton, W. F.: The Falling Drop Method of Determining Specific Gravity, J. Biol. Chem. **69**:625 (Aug.) 1926; The Falling Drop Method of Determining Specific Gravity (Some Clinical Applications), J. A. M. A. **88**:91 (Jan. 8) 1927.

of a drop of blood serum of known size, through a definite distance, in a mixture nonmiscible with the serum. Its rate of fall depends on its density which can be calculated easily as soon as the rate of fall of a similar drop of standard solution of known density (released under identical conditions) is available for comparison.

This study was undertaken to learn the relative reliability of the falling drop method of determining specific gravity as compared with its determination by weight, by the total solid content of the plasma and by the plasma protein on refractometric analysis, the specific gravity being considered an index to the degree of dehydration. Previous investigation showed that the falling drop method made it readily possible to observe changes in the specific gravity of the blood serum of patients following the administration of whole blood, dextrose and salt solutions intravenously, of dextrose and salt solutions intraperitoneally and of salt solutions subcutaneously. Of the sixty-eight specimens of blood examined, eight were from clinically normal children, and the others were from patients in whom it was believed that some alteration might be found in the water content of the blood plasma.

Blood serum appeared more adaptable to the various measurements desired than did whole blood, which coagulates rapidly, and in which, before clotting, an even distribution of the cellular elements is difficult to obtain in the various samples separated from the initial specimens. Then, too, greater accuracy seemed possible when one worked carefully with blood serum than hurriedly with whole fresh blood before coagulation occurred. The use of an anticoagulant would introduce another factor in the procedure, with the correspondingly greater probable error in the results obtained. Of most importance in the use of blood serum, however, is the fact that since water is lost from the plasma much more extensively than from the cells, a greater variation in water content is present for measurement in the serum alone than in an equal volume of a mixture of serum and blood cells. Specimens of venous blood were used rather than those obtained by skin puncture, in which the proportion of tissue fluids varies, influencing the resultant mixture of blood and tissue fluid to a variable and an undeterminable extent. Thus, simplicity and accuracy indicated the use of blood serum rather than fresh uncoagulated whole blood.

The whole blood was permitted to clot in tightly corked centrifuge tubes. The clot was broken up, and after the specimen was centrifugalized, the supernatant serum was removed immediately by pipet. The various observations were made before hemolysis of the red blood cells or evaporation of the serum, and also probably before change in the distribution of the electrolytes had occurred.

TABLE 1.—*Analyses of Blood Serum to Obtain Specific Gravity by Falling Drop and Weight Methods, and to Measure Total Solids and Serum Protein*

	Specific Gravity		Total Solids Content	Serum Protein Content
	Falling Drop Method	Weight Method		
1	1.0241	1.0216	0.0781	6.97
2	1.0183	1.0175	0.0561	4.65
3	1.0202	1.0206	0.0627	5.23
4	1.0177	1.0154	0.0522	4.35
5	1.0211	1.0202	0.0713	6.34
6	1.0209	1.0141	0.0687	6.22
7*	1.0237	1.0208	0.0776	7.20
8*	1.0235	1.0178	0.0754	6.45
9	1.0225	1.0222	0.0742	6.45
10	1.0218	1.0157	0.0688	6.11
11	1.0214	1.0151	0.0673	5.70
12	1.0185	1.0167	0.0666	5.58
13	1.0148	1.0141	0.0417	3.06
14	1.0178	1.0215	0.0570	4.58
15	1.0213	1.0196	0.0680	5.81
16	1.0197	1.0133	0.0602	5.23
17	1.0195	1.0166	0.0696	5.23
18	1.0191	1.0229	0.0603	5.28
19	1.0227	1.0173	0.0701	6.34
20	1.0233	1.0197	0.0732	6.74
21	1.0227	1.0217	0.0709	6.45
22	1.0222	1.0201	0.0708	6.39
23	1.0221	1.0231	0.0693	6.39
24	1.0174	1.0155	0.0593	5.52
25*	1.0253	1.0274	0.0822	7.43
26*	1.0222	1.0174	0.0723	6.45
27*	1.0261	1.0226	0.0900	8.79
28	1.0235	1.0140	0.0757	6.62
29	1.0251	1.0193	0.0912	8.30
30	1.0280	1.0142	0.0545	4.58
31	1.0195	1.0144	0.0621	5.06
32	1.0229	1.0198	0.0700	5.52
33	1.0215	1.0149	0.0685	6.34
34*	1.0249	1.0218	0.0815	7.55
35	1.0215	1.0160	0.0660	5.75
36	1.0214	1.0176	0.0639	5.58
37	1.0239	1.0253	0.0699	5.87
38	1.0244	1.0211	0.0798	7.26
39	1.0229	1.0211	0.0752	7.14
40	1.0236	1.0217	0.0752	7.03
41	1.0228	1.0208	0.0723	6.34
42	1.0221	1.0203	0.0707	6.39
43	1.0287	1.0264	0.0961	10.00
44	1.0283	1.0241	0.0920	8.79
45	1.0272	1.0257	0.0888	8.49
46*	1.0235	1.0210	0.0768	7.55
47	1.0248	1.0202	0.0808	7.61
48	1.0249	1.0159	0.0742	6.39
49	1.0209	1.0180	0.0647	5.58
50	1.0207	1.0176	0.0649	5.52
51	1.0301	1.0303	0.1078	10.27
52	1.0215	1.0181	0.0697	5.58
53	1.0206	1.0180	0.0631	5.64
54	1.0223	1.0196	0.0707	6.22
55	1.0229	1.0197	0.0723	6.39
56	1.0203	1.0134	0.0717	5.40
57*	1.0246	1.0221	0.0798	7.26
58	1.0195	1.0152	0.0586	4.95
59	1.0273	1.0273	0.0927	10.74
60	1.0230	1.0228	0.0768	7.97
61	1.0236	1.0218	0.0793	7.15
62	1.0276	1.0254	0.0936	8.67
63	1.0263	1.0266	0.0890	8.37
64	1.0253	1.0257	0.0770	8.67
65	1.0266	1.0258	0.0889	8.37
66	1.0258	1.0229	0.0870	8.24
67	1.0262	1.0231	0.0882	8.07
68	1.0253	1.0218	0.0874	8.19

* Normal specimen.

The serum protein content was determined by the familiar refractometric method of analysis. The total solids were measured after drying in an electric oven at from 95 to 100 F. for twenty-four hours, and cooling in a calcium chloride desiccator. The specific gravity was obtained by the weight of 1 cc. of serum before desiccation, and also of samples of the same specimens of blood serum, by the falling drop method devised by Barbour and Hamilton.

The following analysis shows the relative accuracy of these methods of obtaining physical measurements, and suggests that the specific gravity as determined by the falling drop method is the most satisfactory index of the water content of the blood serum.

As shown by table 2 and chart 1, the range of dispersion of all the specimens is essentially the same, indicating that both the falling drop and weight methods of determining specific gravity are capable of registering

TABLE 2.—*Dispersion of Specimens of Blood Serum Tested to Obtain Specific Gravity, Total Solids Content and Serum Protein*

	Falling Drop	Weight	Total Solids	Serum Protein
Dispersion of all specimens				
High	1.0301	1.0303	0.0961	10.74
Low	1.0148	1.0133	0.0417	3.06
Range of dispersion	1.0153	1.0170	0.0544	7.68
Dispersion of normal specimens				
High	1.0261	1.0274	0.0900	8.79
Low	1.0222	1.0174	0.0723	6.45
Range of dispersion	1.0039	1.0100	0.0177	2.34
Percentage of total area of dispersion of all specimens included within range of normals	25.5	58.8	30.5	32.5
Percentage of all specimens lying within range of normals	44.1	72.1	63.3	44.1

measurements within the same maximum and minimum extremes. However, the dispersion of the normal cases covered a range of only 0.0039 specific gravity when determined by the falling drop method, whereas when determined by weight, the range of the normal specimens was 0.01, or 2.6 times greater than with the drop method. This range of dispersion of the normal specimens represented a zone of 25.5 per cent of the area of maximum dispersion of all the cases when measured by the falling drop method. By the weight method, the zone of dispersion of the normal specimens represented 58.8 per cent of the range of maximum dispersion of all cases. The zone of normal dispersion by the falling drop method contained 44.1 per cent of all the specimens examined, whereas the much wider normal zone, by the weight method contained 72 per cent of all the specimens (chart 2).

By a similar analysis, the total solid content showed a zone of dispersion of the normal specimens which was 32.5 per cent of the maximum range of dispersion for all specimens. Within this normal zone lay 44.1 per cent of all the cases.

Determinations of serum protein, when analyzed in the same manner, showed a zone of dispersion of the normal cases which was 30.5 per cent of the maximum range, and contained 63.3 per cent of all the specimens examined.

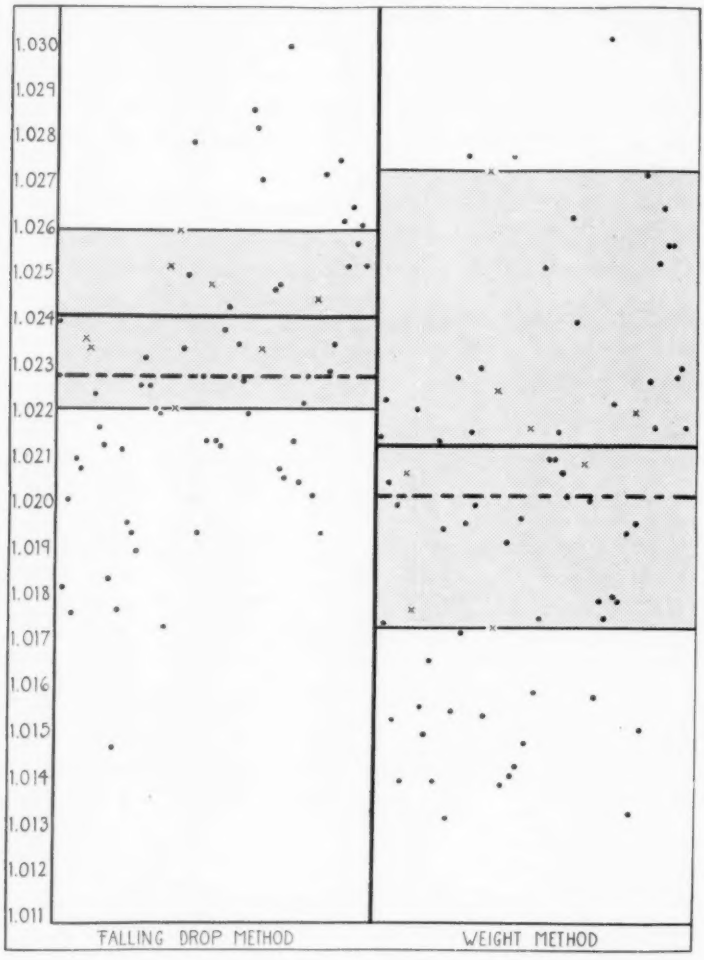

Chart 1.—Range dispersion of the specific gravity of all specimens by the falling drop method and by the weight method. Crosses indicate the specific gravity of normal specimens; dots, the specific gravity of the other specimens; shaded zone, the range of dispersion of the normal specimens; solid line, the average specific gravity of normal specimens; broken line, the average specific gravity of all specimens.

In the scatter diagram, determinations of the specific gravity by the falling drop and the weight methods are charted in the same order, so

that it is possible to identify the corresponding measurements on the individual specimen by both methods.

The apparent great difference in relative accuracy in the same type of gravimetric measurements of the specific gravity and of the total solids on identical specimens seems due to the process of desiccation. The total error in weighing 1 cc. of serum consists partly of the error in the total solid content of the unit volume, and partly of the error in

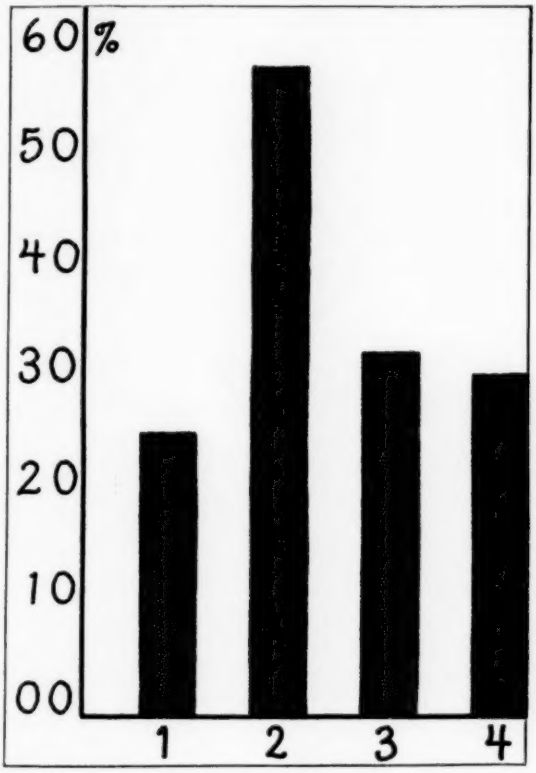

Chart 2.—Range of dispersion of the normal specimens represented in the percentage of the maximum dispersion of all the specimens. Column 1 indicates the specific gravity determined by the falling drop method; column 2, the specific gravity determined by the weight method; column 3, the total solids content; column 4, the serum protein content.

weighing the fluid content of the specimen. By desiccation, the fluid content is removed, and the total error reduced to that incident to weighing alone the total solid content of the original unit volume. Owing to the water content of the solution, a variation of a unit of weight of the solution is equivalent to a variation of less than the same unit of weight in the total solid content of the same volume of solution.

The pipet used in measuring all specimens of the serum for the specific gravity by weight was calibrated to deliver 1 cc. of water. Blood serum is more viscid than water, so that, probably a little less than 1 cc. of serum was actually delivered, owing to the adherence of serum to the sides of the pipet. This may explain why the general level of the specific gravity was slightly lower when obtained by weight than when obtained by the falling drop method.

Thus, the narrower zone of dispersion in the normal cases, when determinations were made by the falling drop method, suggests that this procedure is considerably more accurate than the other types of physical measurements made on samples of identical specimens of blood serum. This method has the additional value of being a simple, rapid procedure, requiring only a small quantity of blood, and it lends itself admirably to clinical application for repeated observations in following the course of a patient under treatment.

In general, the patients exhibiting clinically the most marked dehydration had blood serum of higher specific gravity, greater total solid content and a larger percentage of serum protein than the specimens from normal patients.

CONCLUSIONS

1. The falling drop method is the most accurate of the several methods compared for measuring the water content in determining the specific gravity of the blood serum.

2. The blood serum of patients exhibiting clinically the most marked dehydration had a higher specific gravity, a greater total solid content and a larger percentage of serum protein than the specimens from normal patients.

3. The falling drop method of determining specific gravity is a procedure of clinical value, owing to its simplicity, accuracy and rapidity.

THE USE OF SCARLET FEVER ANTITOXIN*

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Four years have elapsed since the introduction of concentrated scarlet fever antitoxin prepared according to the methods of the Dicks and of Dochez. During that time numerous reports have been published regarding the value of scarlet fever antitoxin. Some observers have declared the serum a "specific" in the treatment of scarlet fever and recommend giving the antitoxin in every case.[1] Some have questioned the value of the serum in the milder types,[2] while others have believed the serum had little, if any, therapeutic value.[3]

In this study of 492 cases of scarlet fever, an attempt has been made to determine in what cases the use of scarlet fever antitoxin is indicated, and what results may be looked for in regard to the course of the disease and the prevention of complications.

This report includes all the patients admitted to the Municipal Contagious Disease Hospital within a period of six months (January to June) having a definite diagnosis of scarlet fever of not more than four days' duration. The majority of the patients were admitted on the second and the third day of the disease. The serum used was that prepared according to the Dicks' method, with the exception of nine cases in which the Dochez serum was substituted. The antitoxin was given intramuscularly, each patient receiving a therapeutic dose of 10 cc., sufficient to neutralize more than 300,000 skin-test doses of toxin. In a few instances, this dose was repeated. Only those patients who had been given antitoxin on or before the fourth day of the disease were considered as having been treated with serum.

Each patient was classified clinically on admission as having a mild, a moderately severe or a severe case of scarlet fever. The severity was dependent on the degree of toxemia. In determining this factor, the appearance of the throat proved to be the most reliable index. A marked redness and swelling involving the tonsils, the uvula, the soft

* Submitted for publication, Sept. 8, 1928.

* From the Municipal Contagious Disease Hospital, Department of Health, Chicago.

1. Platou, E. S., and Collins, Loren: Scarlet Fever, A Clinical Study in Its Prevention and Serum Treatment, Arch. Pediat. **43**:707, 1926.

2. Park, W. H.: Scarlet Fever, Etiology, Prevention, Antitoxic Treatment, J. A. M. A. **85**:1180 (Oct. 17) 1925.

3. Graham, R. H.: Dochez Scarlet Fever Antitoxin in 31 Cases, J. A. M. A. **85**:95 (July 11) 1925.

palate and the walls of the pharynx, sometimes sufficient to cause respiratory embarrassment, characterized the severe type. A filmy, loosely attached false membrane was frequently present in the fauces in the severe cases. The degree of temperature, especially in children, was an unreliable index in determining the degree of severity. The extent and the severity of the eruption usually varied with the severity of the disease, so that in some cases it was an aid in the classification. Patients with an early profuse purulent nasal discharge frequently showed a considerable degree of toxemia and were classified as having severe scarlet fever.

EFFECT OF SERUM ON THE CLINICAL COURSE

Approximately 60 per cent of the cases classified as severe showed some improvement following the use of scarlet fever antitoxin. This improvement was evidenced chiefly by a subsidence in the toxic manifestations. The patient felt more comfortable, the throat was less swollen and the angina less painful. A lowering of the temperature and a fading of the rash were somewhat characteristic. In the cases in which delirium occurred, the conscious state was restored. These changes, when they occurred, took place in from twenty-four to thirty-six hours after the serum was given. In the mild and moderate types, definite improvement could not be determined following the use of antitoxin.

Reasons for the failure of scarlet fever antitoxin to give beneficial results in some cases have been advanced: namely, that the dosage was insufficient and that the serum was given too late in the course of the disease. Probably the best explanation, however, is that given by Park, who said that "the causative strain in cases which do not respond to antitoxin is different from that used in producing the scarlet fever antitoxin."[4] In favor of this theory is the fact that cases that do not respond to treatment with antitoxin give negative results also in the Schultz-Carlton blanching test when the same type of serum is used in making the test as is used therapeutically.

EFFECT OF SERUM ON THE COMPLICATIONS

Probably the most noteworthy claim that has been advanced favorable to the use of scarlet fever antitoxin has been that it materially lessens the number and the severity of the complications.[5] In endeavoring to determine the effect of any treatment on the complications of scarlet

4. Eley, R. C.: Scarlet Fever Antitoxin, Am. J. Dis. Child. **35**:14 (Jan.) 1928.

5. Gordon, J. E.: Treatment of Scarlet Fever with Streptococcus Antitoxin, J. A. M. A. **88**:382 (Feb. 5) 1927.

fever, one should bear in mind that the complications of this disease are subject to wide variations and may be influenced by numerous factors. The "genus epidemicus" that Brenneman [6] aptly described in relation to throat infections in children is equally a factor in scarlet fever. He said:

> The majority of cases run a relatively benign course. A bilateral cervical adenitis, varying in degree, accompanies nearly all of the cases. Of the more serious complications, otitis media is the most frequent. In certain epidemics, it is rare and mild. In others, it is the rule and is often of uniformly grave character. Whether we have as an explanation for the variations a different organism, or an organism of varying virulence, or a peculiar meteorological condition remains to be determined. The individual seems to play a small part in the matter.

TABLE 1.—*Incidence of Complications According to Severity*

Case Groups	Number of Cases	Cases Without Complications	Percentage Without Complications	Cases With Complications	Percentage With Complications
Not Treated with Serum (Control)					
Mild	92	72	78	20	22
Moderate	144	100	70	44	30
Severe	39	15	38	24	62
Total	275	187	68	88	32
Treated with Serum					
Mild	27	19	70	8	30
Moderate	119	78	66	41	34
Severe	71	31	44	40	56
Total	217	128	59	89	41

In this series of cases, apart from the severe cases, scarlet fever antitoxin seemed to play little, if any, rôle in lessening the number or the severity of the complications.

Table 1 shows the incidence of complications in the group treated with scarlet fever antitoxin to be 41 per cent, as compared with 32 per cent in the group not treated with serum. When the cases of severe type alone are considered, however, 56 per cent of the group treated with serum developed complications, as compared with 62 per cent of the group used as controls, a difference of 6 per cent in favor of treatment with serum. In view of the fact that the group treated with serum included much the larger number of severe cases, this difference of 6 per cent speaks favorably for the use of antitoxin in cases of scarlet fever of severe type.

6. Brenneman, Joseph: Throat Infections in Children, Arch. Pediat. **42**:145, 1925.

Table 2 gives the percentage incidence of each complication as it occurred in the group of controls and the group treated with serum. Cervical adenitis was considered a complication only when it developed secondarily after the first week of the disease. The occurrence of otitis media was equally divided between the group of the controls and the serum-treated group. The incidence of mastoiditis was higher in the group of the controls, but mastoiditis is a complication the occurrence of which is not infrequently dependent on early and proper treatment of otitis media, and it is doubtful if the administration of serum plays any part in its prevention. Hemorrhagic nephritis, while not a common complication, occurred with the same frequency in the group of the con-

TABLE 2.—*The Complications of Scarlet Fever*

Case Groups	Number of Cases	Otitis Media	Persistent Secondary Cervical Adenitis	Mastoiditis	Persistent Rhinitis	Hemorrhagic Nephritis	Albuminuria	Arthritis	Bronchitis	Bronchopneumonia	Blepharitis and Ethmoiditis	Urticarial Seroreaction Rashes	Generalized Seroreactions
Not Treated with Serum (Control)		%	%	%	%	%	%	%	%	%	%	%	%
Mild.....	92	4.3	7.0	....	3.0	...	1.0	...	1.9	...	...	..	..
Moderate.....	144	11.0	25.0	1.1	10.0	4.8	1.0	1.4	2.7	1.0	0.9	..	..
Severe.....	39	25.6	33.3	10.0	11.0	5.1	5.1	2.5	5.1	5.1	5.0	..	..
Total.....	275	10.9	20.0	2.6	8.3	3.3	2.0	1.0	3.0	1.5	1.0	..	..
Treated with Serum													
Mild.....	27	7.4	14.8	....	....	...	1.0	...	...	...	...	20.0	4.0
Moderate.....	119	9.2	24.3	1.0	5.0	3.3	1.0	2.5	...	2.0	1.0	31.6	6.7
Severe.....	71	22.5	32.0	2.8	4.2	7.0	1.4	7.0	2.8	3.0	2.8	24.0	12.6
Total.....	217	13.3	25.0	1.4	4.3	4.1	2.0	3.7	2.0	2.0	1.9	27.5	9.0

trols as in the group treated with serum. Here again early proper medical care and diet have been shown to play an important part in the prevention of the complication.[7]

A severe complication that caused not a little anxiety occurred in a sufficient number of cases to deserve special mention. It is designated in table 2 as "blepharitis and ethmoiditis." This complication was characterized by a profuse purulent nasal discharge, a marked unilateral exophthalmos, increased intraocular tension and a red, swollen upper eyelid, causing the eye to remain completely closed for several days. The pain was severe. The temperature remained high (from 103 to 104 F.) for from ten days to two weeks. These patients, all children except one, were examined by a competent otolaryngologist, who concurred in the diagnosis of ethmoiditis. These patients all made a good recovery without operative intervention.

7. Hoyne, A. L.: Treatment of Scarlet Fever, Illinois M. J. **48**:465, 1925.

Cardiac complications were infrequently met with. In not one instance did an acute endocarditis occur as a direct complication during the patient's stay in the hospital. In four cases, however, there was an acute exacerbation of a chronic endocarditis. Heart murmurs were a common occurrence during the first few days of the disease, but almost invariably the murmur disappeared before the time for the patient's release from the hospital.

The scarlet fever antitoxin not uncommonly produced seroreactions, and in some instances produced symptoms of greater severity than the disease for which the antitoxin was used. Of 217 patients treated with serum, 60, or 27 per cent, developed urticarial rashes. Nineteen, or 9 per cent, showed severe generalized seroreactions. In some, the reaction was manifested by an elevation in temperature of from 102 to 105 F., generalized adenopathy, chills and general malaise lasting for three or four days. In two cases, the seroreaction was characterized by marked

TABLE 3.—*Deaths*

	Treated with Serum			Not Treated with Serum		
Type of Case	Number of Cases	Number of Deaths	Death Rate, per Cent	Number of Cases	Number of Deaths	Death Rate, per Cent
Mild	27	0	0	92	0	0
Moderate	119	0	0	144	0	0
Severe	71	4	5.6	39	4	10.2

meningeal symptoms and a temperature as high as 105 F., convulsions, rigidity of the neck, projectile vomiting, a positive Babinski sign and ankle clonus. In both cases, the results of the examination of the spinal fluid were negative. The symptoms lasted for three days and were followed by uneventful recoveries.

Four deaths occurred in the group treated with serum. Three of these, occurring on the fourth, the fifth and the sixth days of the disease, respectively, were due to severe acute toxemia. The fourth was that of a patient in whom septic conditions developed together with bilateral bronchopneumonia, empyema, otitis media and pericarditis with effusion.

There were four deaths in the group not treated with serum. Two were due to severe toxemia in the early stages, a third followed bronchopneumonia, and a fourth was due to streptococcic meningitis complicating otitis media, mastoiditis and lateral sinus thrombosis.

Deaths did not occur in the mild or moderate cases in either the group treated with serum or the group not treated with serum. All the deaths in both groups occurred in the severe cases. The mortality rate in the group not treated with serum, based on the severe cases only, was almost double that in the group treated with serum (table 3).

While this report does not include cases in which treatment with convalescent scarlet fever serum was used, this form of therapy is being used in the hospital in many severe cases. Its use has given rather striking results in lessening the toxic manifestations and has proved somewhat more reliable than scarlet fever antitoxin.

SUMMARY

Scarlet fever antitoxin seemed to exert a beneficial effect in lessening the toxemia of scarlet fever in 60 per cent of the cases classified as toxic or severe.

In the mild and moderate cases, a favorable effect was not observable, and the use of scarlet fever antitoxin in these cases unnecessarily exposed the patients to the danger of severe seroreactions.

The incidence of complications in cases of the severe type was lower in the group treated with serum than in the group not so treated.

The incidence of complications in cases of the mild and the moderate types was not lowered in the cases in which scarlet fever antitoxin was given.

The mortality rate based on severe cases only in the group that did not receive antitoxin was almost double that of the group in which scarlet fever antitoxin was used.

THE RELATION OF THE TONSILS TO ACUTE RHEUMATISM DURING CHILDHOOD

A STUDY OF FOUR HUNDRED AND THIRTY-NINE CHILDREN WITH ACUTE RHEUMATISM *

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During recent years, numerous surveys have been made on the relationship of the tonsils to rheumatic manifestations. The interpretation of these results has not been uniform, but most authorities concede that the tonsils bear a certain relation to rheumatism and to rheumatic endocarditis. A more accurate understanding of this relationship is desirable.

In this survey, 439 children who had acute rheumatism were studied, and a special effort was made to determine the relationship of the rheumatic attacks to the presence or absence of the tonsils. The term "acute rheumatism" is used in order to include the cases of children who did not have the classic attacks of rheumatic fever, but in whom there had been definite involvement of the joints and muscles. Two hundred and forty-one of the children studied had characteristic attacks of rheumatic fever, 138 had acute pains in the joints but no redness or swelling, and 60 presented rheumatic manifestations that could be described as growing pains or pains in the muscles. Cases of chorea or rheumatic endocarditis were not included in the study unless there had been evidence of the involvement of joints or muscles.

Acute rheumatism occurs infrequently before the age of 5. Rheumatic infection occurs in young children more often than is generally supposed, although manifestations in the joints and muscles are not always evident. Cases of rheumatic endocarditis, which were not included in this study, were observed in children less than 5 years of age in whom a history of acute rheumatism could not be obtained. The period from 8 to 15 years of age seems to be the most vulnerable for this infection. All these children developed their first and subsequent attacks of rheumatism during the period when a large group of children in Rochester were under observation; in this group were children on whom tonsillectomy had been performed, and others on whom it had not been performed. Definite information concerning the number of children in the various age groups on whom it had been performed was obtained for the period of time included in the rheumatic history of this group. Efforts have

* Submitted for publication, Sept. 24, 1928.

been made to answer the following questions in this study: 1. Does acute rheumatism develop for the first time as frequently in children whose tonsils have been removed as in those not operated on? 2. Do recurrent attacks occur as often in children whose tonsils have been removed after one attack of rheumatism as when a tonsillectomy has not been performed? 3. Do recurrent attacks occur as often in children who have their first attack after the tonsils have been removed? 4. Does endocarditis occur as frequently in children who have had acute rheumatism following a tonsillectomy as when the tonsils have not been removed?

The figures in table 2 seem to indicate that the first attack of acute rheumatism occurs much more commonly in children whose tonsils have

TABLE 1.—*Occurrence of First Attack of Acute Rheumatism Among 439 Children*

Age of Children	Number of Cases
Less than 5 years	38
From 5 to 10 years	126
From 10 to 15 years	239
More than 15 years (16 and 17 years)	36

TABLE 2.—*Appearance of First Attack of Acute Rheumatism in Relation to Removal of Tonsils in 439 Children*

Age of Children	Before Tonsillectomy	Tonsils In, Not Removed Later	After Tonsillectomy	Tonsils In	Tonsils Out
Less than 5 years	9	27	2	36	2
From 5 to 10 years	44	60	22	104	22
From 10 to 15 years	94	57	88	151	88
More than 15 years (16 and 17 years)	12	13	11	25	11
Total number of cases	159	157	123	316	123

not been removed. It must be remembered, however, that tonsillectomy has not been performed on the majority of children in a community; therefore, one would expect the greater incidence of a first attack of acute rheumatism in these cases.

Fortunately, data were available concerning the number of children whose tonsils had been enucleated and those not operated on. The figures were based on the results of a survey made on 48,000 children in Rochester two years before. The records showed that 42 per cent of the children between the ages of 5 and 15 years had undergone tonsillectomy and that 58 per cent had not. The group of rheumatic children between the ages of 5 and 15 years studied at the time of their first attack belonged to this large group of school children. The control group of children between the ages of 5 and 15 who were not operated on was 16 per cent larger than the group of children of the same age who had their tonsils removed. Of the entire group studied,

365 children developed acute rheumatism between the ages of 5 and 15 years. Two hundred and fifty-five developed acute rheumatism before and 110 after the tonsils were removed; since there were 16 per cent more children whose tonsils had not been removed, one could justly expect the condition to occur in 151 instead of in 255.

In an entire community, the percentage of children less than 5 years of age whose tonsils have been removed is small. It would be natural, therefore, to expect a higher incidence of acute rheumatism. In the group of thirty-eight children who developed acute rheumatism before the age of 5 years, thirty-six cases occurred in children whose tonsils had not been removed and two in children following the removal of the tonsils. The group of persons more than 15 years of age is small, since it includes only those subjects who had their first attack of acute rheumatism at 16 or 17 years of age. When one considers that at this age nearly 50 per cent of the subjects in Rochester have had their tonsils

TABLE 3.—*Incidence of Recurrent Attacks of Acute Rheumatism with Reference to Removal of the Tonsils in 439 Children*

Age of Children	Before Tonsillectomy	After Tonsillectomy (First Attack Before Tonsillectomy)	After Tonsillectomy (First Attack After Tonsillectomy)	No Tonsillectomy
Less than 5 years	3	1	2	6
From 5 to 10 years	10	10	14	18
From 10 to 15 years	19	19	13	18
More than 15 years (16 and 17 years)	3	4	2	3
Total number of cases	35	34	21	45

removed, it is interesting that twenty-five of the thirty-six persons in the group had not been operated on, while eleven had their first attack after enucleation of the tonsils.

This marked difference in the incidence of the disease suggests that the presence of tonsils predisposes to the first attack of acute rheumatism, and, conversly, that the removal of the tonsils offers considerable hope of escape from this infection.

The assumption that acute rheumatism is less likely to occur for the first time in children whose tonsils have been removed gives rise to the second question: Do recurrent attacks appear as often in children whose tonsils are removed after the first attack as in those who are not operated on? The question of recurrence is extremely important, for permanent cardiac involvement commonly follows second or subsequent attacks.

There were 316 children who had their first attack before the tonsils were removed. Of that number, eighty had one or more recurrent attacks of acute rheumatism before their tonsils were removed, and fifty-six had their second attack after enucleation of the

tonsils. In thirty-four children, however, the first attack occurred before tonsillectomy. Recurrent attacks are by no means prevented when tonsillectomy is performed after the first attack, but they are likely to occur about 10 per cent less often than in the children who are denied an operation after the first attack.

The third query is: Do recurrent attacks come as often in children who had their first attack after the tonsils had been removed as in children who had their first attack before tonsillectomy? On the average, approximately three years have elapsed since the last attack in this group. It is probable that several children in both groups will have further recurrent attacks. Since both the children who have had the tonsils removed and those who have not are affected, the percentage of recurrences may not be greatly altered even during a period of five or ten years. Thirty-one of 123 children who had acute rheumatism for the first time after tonsillectomy had recurrences. Thirty-four of 159 children who had the tonsils removed after the first attack of rheumatism had recurrences. Twenty-five per cent of the children who

TABLE 4.—*Incidence of Carditis in 439 Rheumatic Children*

	Number of Cases	Per Cent
Developed before removal of tonsils	126	40
Developed after removal of tonsils	48	39

had the first attack after tonsillectomy had recurrences, while the percentage of recurrences in children who were operated on after their first attack was 20 per cent. One must conclude from these figures that rheumatism developing for the first time in a child who has had the tonsils removed is more likely to recur than in the patient who is infected before tonsillectomy.

The fourth query in this study is: Does endocarditis occur as frequently in children who develop acute rheumatism after tonsillectomy as in those who are operated on?

Forty-eight of 123 children who had their tonsils removed before the first attack of rheumatism developed rheumatic endocarditis. The incidence of the disease was 39 per cent, which is only slightly less than the incidence in children of this group who have not been operated on. On the basis of a previous report concerning the school children in Rochester, evidence of rheumatic carditis was found in 2.2 per cent of those operated on and in 2.9 per cent of those not operated on. Rheumatic carditis existed before the removal of tonsils in a number of children. There is, therefore, a considerable difference between the incidence of carditis in the two groups. Any rheumatic infection with the exception of chorea, however, in a child whose tonsils have been

removed is almost as likely to lead to rheumatic carditis as when the tonsils are present. The lessened incidence of carditis in children who have had tonsillectomies performed is due to a lessened incidence of rheumatism.

A discussion of chorea is not within the scope of this paper. Chorea as a complication in rheumatism occurred with equal frequency in children operated and not operated on, but carditis following chorea was less common among those whose tonsils had been removed.

COMMENT

While the search for the causative factor in rheumatism is going on, exhaustive investigations have been undertaken, especially in England,[1] analyzing such factors in the disease as social conditions, environment and contacts. The tonsils also were considered. It was found in England [2] that neither cutting nor enucleation of tonsils gave any guarantee of immunity from rheumatism. Of 295 rheumatic children who had their tonsils surgically treated, 43.7 per cent subsequently developed rheumatism for the first time, although in half the cases, the tonsils had been enucleated completely. These reports did not present data on the incidence of acute rheumatism in groups of children operated and not operated on for removal of the tonsils. The general consensus, however, is that tonsillectomy offers some protection against initial and recurrent attacks of rheumatism. Similar conclusions have been reached by investigators in this country, principally Ingerman and Wilson,[3] St. Lawrence,[4] Mackie [5] and Robey.[6] Additional evidence is desirable to corroborate these opinions. If enucleation of tonsils safeguards even a small percentage of children against rheumatism, it is valuable and should be practiced in selected cases; if the likelihood of recurrence is lessened, all persons with rheumatism should have the benefit of this operation. When the etiologic factor is known definitely, this procedure may seem unnecessary.

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1. Social Conditions and Acute Rheumatism, London, Medical Research Council, 1927.

2. Acute Rheumatism in Children in Its Relation to Heart Disease, London, Ministry of Health, 1927.

3. Ingerman, Eugenia, and Wilson, May G.: Rheumatism: Its Manifestations in Childhood Today, J. A. M. A. **82**:759 (March 8) 1924.

4. St. Lawrence, William: The Effect of Tonsillectomy on the Recurrence of Acute Rheumatic Fever and Chorea, J. A. M. A. **75**:1035 (Oct. 16) 1920.

5. Mackie, T. T.: Rheumatic Fever: An Analytical Study of Three Hundred and Ninety-Three Cases of Rheumatic Fever and Eighty-Nine Cases of Chorea, Am. J. M. Sc. **172**:199 (Aug.) 1926.

6. Robey, William H., and Freedman, Louis M.: The Effects of Tonsillectomy on the Acute Attack and Recurrence of Rheumatic Fever, Boston M. & S. J. **196**: 595 (April 14) 1927.

Sufficient evidence is available now to prove that acute rheumatism is not necessarily the result of a tonsillar infection. In the foregoing series of cases, a number of children who developed a severe rheumatic infection with carditis did not have tonsillar tissue. The tonsils are not the only avenue of infection, but it is not sound judgment to consider only the cases in which the patients developed rheumatism after tonsillectomy had been performed. The incidence of the disease during the same period of time in children who have been operated on for removal of the tonsils must be compared with those who have not. A similar study must be made of the recurrent attacks of rheumatism.

SUMMARY

The analysis of the 439 rheumatic children discloses the following facts:

1. The most susceptible age for the first attack of rheumatism is between 8 and 14 years.

2. Nearly twice as many children in the community studied developed the first attack of rheumatism when the tonsils were still present.

3. Recurrent attacks of rheumatism occurred 10 per cent less often in children who had their tonsils removed after the first attack of rheumatism than in those whose tonsils were not removed.

4. The incidence of carditis as a complication in acute rheumatism was nearly as frequent in children who had undergone a tonsillectomy as in those who had not.

5. Chorea occurred as a complication in acute rheumatism with equal frequency in children operated and not operated on, but the association of carditis with chorea was less in children whose tonsils had been removed.

6. Tonsils are the avenue of infection in many cases of rheumatism and bear a definite relationship to this disease. Their removal should be advocated in the rheumatic and potentially rheumatic child until more is known of the etiology of rheumatism.

DETERMINATIONS OF THE AMOUNTS OF BASE, CHLORIDE, FREE AND TOTAL ACIDITY

IN THE GASTRIC CONTENTS OF CHILDREN ON WHOM GASTROSTOMY HAD BEEN PERFORMED IN THE GASTRIC CONTENTS OF FASTING NEW-BORN INFANTS *

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AND

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The object of the work outlined in this paper was to determine the amounts of fixed base, total chloride, free acidity and total acidity in the gastric contents of children and of fasting new-born infants. Such determinations have not been recorded, to our knowledge, from cases in which gastric fistulas occur at the same time as patent esophagi. Nor have such determinations been recorded for the gastric contents of new-born infants previous to their ingestion of milk or water. The removal of the contents through a gastric fistula offers a means of eliminating the errors that have been shown to occur with the passage of the stomach tube.[1] The results of these examinations, it was felt, would afford a more complete picture of the electrolyte balance in the contents of the fasting stomach, and of the stomach stimulated to secretion by an alcohol test meal, as well as a comparison with the electrolyte balance in the blood. We were also fortunate in obtaining, for comparison, data on the gastric contents of an adult who had both a gastric fistula and a patent esophagus.

REVIEW OF THE LITERATURE

Rosemann [2] made some determinations of the total base on two large samples of gastric juice collected from dogs by the "sham feeding" method of Pavlov. He found the concentration of fixed base in these samples to be 20 milliequivalents, while the concentration of chloride was about 147 milliequivalents. Gamble and McIver,[3] using

* Submitted for publication, Sept. 28, 1928.

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1. Kahn, G., and Stokes, J., Jr.: The Effect of the Passage of a Stomach Tube on Titratable Acidity and p_H of Gastric Contents, Am. J. Dis. Child. **32**:667 (Nov.) 1926.

2. Rosemann, R.: Arch. f. d. ges. Physiol. **118**:467, 1907.

3. Gamble, J. G., and McIver, M. A.: Proc. Soc. Exper. Biol. & Med. **23**: 439 (March) 1926.

dogs, made an interesting study of the contents of gastric pouches that furnished secretion from both the fundic and the pyloric ends of the stomach, after stimulation by diets rich and poor in protein. Their conclusion, in brief, was that the fixed base in gastric contents varies considerably in amount, depending on the type of meal and other factors, while the chloride concentration remains at a fairly constant level, equivalent in round numbers to the total base in the blood plasma. Thus, they felt that in the electrolyte balance the chloride was, on the one hand, the constant factor in gastric contents; and that the base, on the other hand, was the constant factor in the blood. Following the completion of our studies, two other articles appeared. Polland, Roberts and Bloomfield [4] analyzed the gastric contents both before and after stimulation with histamine, in twenty-two ward patients with varying diagnoses. They determined by fractional analyses the volume of the secretion, and the concentration and the total secretion of chloride, base and nitrogen. From their results they decided that the increase in the titratable acidity following stimulation with histamine was due more to the increased output of chloride than to the decreased output of base. Bulger, Stroud and Heideman [5] studied the concentrations of base, chloride and free hydrochloric acid and the total acidity in the gastric juice of persons who had ingested 400 cc. of water, to which had been added 1 cc. of a solution of phenolsulphonphthalein for the purpose of correcting dilution errors. They found, in agreement with Gamble and McIver, that there was little change in the concentration of chloride during the secretion of acid, but that the total base fell in proportion to the increase in the amount of acid; the acid thus being liberated by a retention of the base.

The concentration of chloride in gastric contents has been determined by numerous investigators, few of whom, however, have attempted to link their results with the chloride content or base content of the blood. Berglund, Wahlquist and Sherwood,[6] examining gastric secretion in ward patients after secretion had been stimulated with histamine, felt that almost all the chloride was present as free hydrochloric acid, and that its concentration was practically equivalent to the base content of the blood. They were particularly interested in the views of a group of English writers: Bolton and Goodhart,[7] and Baird,

4. Polland, W. S.; Roberts, A. M., and Bloomfield, A. L.: J. Clin. Investigation **5**:611, 1928.

5. Bulger, H. A.; Stroud, C. M., and Heideman, M. L.: J. Clin. Investigation **5**:547, 1928.

6. Berglund, H.; Wahlquist, H., and Sherwood, K. K.: Proc. Soc. Exper. Biol. & Med. **24**:927, 1927.

7. Bolton, C., and Goodhart, G. W.: Lancet **1**:420 (March) 1922.

Campbell and Hern,[8] who had been gathering data concerning the theory of Boldyreff.[9] This theory proposed a constant control of the gastric acidity by a regulated opening and closing of the pylorus to allow regurgitation of the alkaline contents of the duodenum. On the basis of this theory and the results of their gastric analyses, they stressed the importance of the estimation of the amount of the chloride rather than of the acidity in determining gastric secretory function.

MATERIAL AND METHODS

Material.—Seven children were studied; all ranging between the ages of 3 and 8 years, and possessing gastric fistulas and patent esophagi. One man with a similar condition was also examined for the purpose of comparison. All these subjects had suffered lye strictures of the esophagus and had had gastrostomies performed in order that "retrograde bougies" might be passed into them for the slow dilatation of the strictures. A connecting string between the external nares and the gastrostomy opening, passing through the esophagus, was always present, as well as a large rubber catheter fastened by adhesive tape to the abdominal wound. The children and the adult were in good health. Besides these subjects, fourteen healthy new-born infants were chosen from the Maternity Ward of the University Hospital and similar studies made on them.

Methods.—For the patients on whom gastrostomies had been performed, an alcohol test meal of 25 cc. of water containing 7 per cent alcohol was chosen as giving somewhat the same stimulation to the gastric secretion that food gives while obviating the difficulties that the usual test meal causes in determinations of the amounts of base and chloride. The small volume of this test meal and the delay in collecting the specimen, we felt, would avoid, to a large extent, the dilution of the gastric secretion, which, as Gorham[10] pointed out, has been entirely neglected in the great majority of analyses of gastric contents. The amounts of contents obtained after the test meal were too small to permit entire neglect of the factor of dilution, and on that account the results may be somewhat below the normal figures. The use of dyes to detect the factor of dilution, as advised by Gorham, and later by Bloomfield and Keefer,[11] has distinct advantages when larger test meals are used, or when small "fractional" amounts are obtained and examined soon after the ingestion of the meal. In the present study, it was felt that the use of dyes was unnecessary.

In each instance, the gastric contents were removed through the inlying catheter after a night's fast; the alcohol test meal was then given by mouth and aspirated through the same tube from fifty minutes to an hour after ingestion. The removal of the gastric contents through the fistulas for the determination of the normal concentrations of base, chloride and acidity, has a great advantage over their withdrawal through a stomach tube; for the passage of the tube and its presence in

8. Baird, M. McC.; Campbell, J. M. H., and Hern, J. R. B.: Guy's Hosp. Rep. **74**:23 (Jan.) 1924.

9. Boldyreff, W.: Quart. J. Med. **8**:1, 1914.

10. Gorham, F. D.: The Factor of Dilution in Gastric Analysis, J. A. M. A. **81**:1738 (Nov. 24) 1923.

11. Bloomfield, A. L., and Keefer, C. S.: Method for Continuous Quantitative Estimation of Gastric Secretion and Discharge in Man, Arch. Int. Med. **37**:819 (June) 1926.

the stomach frequently brings about contamination of the contents by saliva and mucus during the aspiration, as shown by Kahn and Stokes.[1] Our subjects were entirely unconscious of the strings that have been mentioned as connecting the nares with the fistulas.

Many authors have emphasized the difficulty of removing the entire gastric contents at each aspiration, and, in our experience, this difficulty could not always be overcome. Gorham[12] called attention to the importance of removing the entire gastric contents in order to obtain the correct values of the concentration; for he found that different small fractions of the gastric contents obtained were not of uniform composition. In order to test how completely the contents of the stomach could be removed by the catheter in the fistula or by the stomach tube, different subjects were given barium meals, and the aspiration of the meals was performed under the fluoroscope while the subjects were shifted to various positions. The tubes could be directed with the help of the fluoroscope, but even under these circumstances removal of the entire contents of the stomach was difficult. Some authors have felt that this difficulty could be disregarded if similar results were obtained from the same subject on different days; but in our experience physical difficulties in aspiration are apt to repeat themselves in the same subject, and thus the analyses may be similar without being correct. Of course, the contents of the stomach are removed more easily and more completely from a subject with a gastric fistula. However, on account of the factors mentioned, we made several determinations on each subject, thus diminishing the degree of error as far as possible.

In removing the contents of the stomachs of the fasting new-born infants, we used a small nasal catheter. The gagging reflex is extremely sluggish in the average new-born infant, and by passing a slender tube through the nose so that little gagging or other discomfort resulted we probably avoided to some extent the alterations in gastric contents which the usual procedure with a stomach tube entails in older children.

Each sample of gastric contents from the children and the infants was examined for the concentration of total base by the method of Stadie and Ross,[13] for the concentration of chloride by the method of Van Slyke[14] and, if sufficient fluid remained, for the free and the total acidity by Töpfer's reagent and phenolphthalein respectively, titrating with tenth-normal sodium hydroxide solution. Duplicate determinations were made for both base and chloride, and at times, as controls, determinations were made on standard solutions. The phosphate in gastric contents is not of sufficient amount to give rise to any marked error in the determinations of amounts of base.

RESULTS

In each case of a child with a gastric fistula, the total quantity of stomach contents removed, both from the fasting stomach and after the alcohol test meal, was small, despite prolonged effort and the shifting of the subject's position. Considering the small test meal and the small size of the stomach, due to the ages of the subjects, we felt that the best results could be obtained by a single removal of the contents, rather than

12. Gorham, F. D.: Variation of Acid Concentration in Different Portions of Gastric Chyme, Arch. Int. Med. **27**:434 (April) 1921.

13. Stadie, W. C., and Ross, E. C.: J. Biol. Chem. **45**:735 (Oct.) 1925.

14. Van Slyke, D. D.: J. Biol. Chem. **63**:523, 1923-1924.

by fractional analyses. As has been mentioned, the barium test meal was given to certain subjects to test whether or not the amounts shown in table 1 represented a complete removal of the contents.

In table 1 are presented the values for the concentrations of base and of chloride in milliequivalents in the gastric contents during fasting and in the contents after a test meal, as well as the few figures that we

TABLE 1.—*Analyses of the Gastric Contents of Children on Whom Gastrostomy Had Been Performed*

	Contents During Fasting					Contents After Test Meal				
			Acids					Acids		
Subject	Chloride	Base	Free	Total	Volume, Cc.	Chloride	Base	Free	Total	Volume, Cc.
	—Milliequivalents per Liter—					—Milliequivalents per Liter—				
1	74.5	78.8	....	....	10	60.5	62.0	....	....	10
	73.6	65.0	....	....	6	30.2	39.0	....	....	5
	67.2	91.0	0	50.0	10	77.5	72.7	24.2	25.6	10
	41.5	97.7	....	....	3.5	....	....	....	....	..
	63.2	67.6	....	....	8	....	....	....	....	..
	33.5	94.8	....	....	4	59.1	63.8	....	....	5
	84.5	88.1	....	....	10	....	....	....	....	5
	53.7	87.0	0	40.0	12	....	....	....	....	..
2	....	142.1	....	....	3.5	....	....	....	....	..
	99.6	92.5	....	....	5	86.1	52.4	....	....	10
	86.4	....	....	....	1	....	....	....	....	..
	104.3	67.1	....	....	15	58.0	21.6	....	....	2.5
	83.8	72.5	....	....	7	....	....	....	....	..
3	....	....	....	....	..	42.1	....	....	....	..
	....	....	....	....	..	65.5	96.6	....	....	20
	65.4	89.4	7.6	39.4	8	52.1	89.5	0	3.2	6
	65.9	81.9	....	....	..	....	....	....	....	..
	82.9	98.2	....	....	..	52.1	62.0	....	....	..
	74.4	89.6	0	18.0	6	54.1	87.1	0	10.6	10
4	81.1	55.8	....	....	6	63.6	74.5	....	....	5
	70.0	68.5	....	....	5	54.7	44.6	....	....	3
	76.0	99.4	8.8	27.6	15	42.0	74.5	0	5.0	10
	83.9	89.5	....	....	25	44.2	55.8	....	....	3
	59.5	86.4	....	....	5	....	....	....	....	..
5	45.2	91.4	....	....	2.5	....	....	....	....	..
	51.0	67.7	5.8	12.6	20	....	....	....	....	..
	56.4	66.6	....	....	..	44.4	77.7	3.6	27.8	10
	74.1	45.1	....	....	..	74.8	94.1	....	....	..
	44.4	58.0	7.4	22.8	9	54.8	38.3	....	....	..
	....	....	....	....	..	95.5	60.2	17.0	28.4	15
6	40.7	67.6	....	....	2	....	182.2	....	....	1
	47.4	60.4	....	....	..	30.2	45.1	....	....	2
7	80.1	76.6	44.4	70.4	30	64.0	77.9	11.4	26.0	10
	58.3	105.7	....	....	..	....	....	....	....	..
	71.5	97.2	20.0	77.4	4	56.6	71.7	....	....	2.5
	82.0	136.9	....	....	3	33.7	54.3	....	....	4

obtained on the free and the total acidity. In order to obtain duplicate results on the base and the chloride, we frequently used up the small amount of gastric contents available, and procured just a sufficient number of determinations of acid contents to give us an idea of their relative importance. As shown, the gastric contents in the great majority of cases contained little, if any, free hydrochloric acid, an observation which is to be expected in view of the ages of the subjects.

In table 2, the determinations of the concentrations of base and chloride, and of the free and the total acidity, can be contrasted with

the corresponding determinations in table 1. The chloride content of the stomach is shown to be somewhat higher in the adult than in the majority of the children, while the figures for the base are about the same. The total quantity of gastric contents is shown to be greater in the adult, as might be expected, and here is noted, also, the appearance of free hydrochloric acid and a greater total acidity.

In table 3 are presented similar determinations with the exception that from only a few infants did we obtain sufficient gastric contents

TABLE 2.—*Analyses of the Gastric Contents from an Adult on Whom Gastrostomy Had Been Performed*

Contents During Fasting					Contents After Test Meal				
		Acids					Acids		
Chloride, Milliequivalents per Liter	Base, Milliequivalents per Liter	Free, Milliequivalents per Liter	Total, Milliequivalents per Liter	Volume, Cc.	Chloride, Milliequivalents per Liter	Base, Milliequivalents per Liter	Free, Milliequivalents per Liter	Total, Milliequivalents per Liter	Volume, Cc.
118.1	59.1	22.2	45.8	20	103.5	44.4	20.4	35.4	30
95.2	....	....	....	25	83.2	60.4	....	....	25
88.4	74.7	....	....	9	....	....	....	....	..

TABLE 3.—*Analyses of the Gastric Contents from Fasting New-Born Infants*

Babies	Chlorides, Milliequivalents per Liter	Base, Milliequivalents per Liter	Free Acids, Milliequivalents per Liter	Total Acids, Milliequivalents per Liter	Volume, Cc.
1.....	97.4	.....	....	....	2
2.....	102.0	111.1	....	....	2.5
3.....	102.4	.....	....	....	2
4.....	101.8	.....	....	....	1.5
5.....	104.5	126.0	....	....	3
6.....	103.8	.....	....	....	2
7.....	120.3	99.2	....	....	8
8.....	120.2	112.8	....	....	2.5
9.....	110.0	153.6	....	....	3.5
10.....	113.8	.....	....	....	1
11.....	109.4	109.2	14.4	17.4	25
12.....	119.7	104.4	57.0	67	...
13.....	102.2	120.4	10.2	19.4	...
14.....	119.2	109.4	13.6	35.8	...
Average..	109.0	116.2	23.8	34.9	

to allow of a test for acidity, as well as for base and chloride. However, such results as were obtained were striking. The gastric contents from most of these infants, we felt, represented the same type of secretion that Pawlow obtained in his "sham feeding" experiments on dogs, for the babies were usually hungry and had been sucking their fists or blankets.

COMMENT

The most striking of the observations on the children with fistulas was that in the great majority of the determinations the concentration of base in milliequivalents exceeded the concentration of chloride. The adult had a greater concentration of chloride than of base, both

during fasting and after the test meal. In the gastric contents of the fasting new-born infants, there was almost an even distribution of the base and the chloride, but when the chloride present as free hydrochloric acid was subtracted from the figure for the total chloride, there was found a quantity of base for the anion of which we cannot at present account. The hydrogen-ion determinations on the gastric contents of these fasting new-born infants [15] invariably attested the presence of considerable quantities of free hydrochloric acid; an amount which is not evident in the gastric contents of the fasting children with gastrostomies.

The excess of base over chloride found in these two groups of cases raises the question as to what anions are combined with the excess base. Bicarbonate and protein may be disregarded in the infants with gastric contents of low p_H.[16] Phosphate can balance probably less than 1 mm. of base per liter, and lactic acid is rarely found in the gastric contents of normal subjects. Information concerning the sulphate in gastric contents was not found.

Our results on the gastric contents of fasting infants did not accord, in many ways, with those obtained by Gamble and McIver; [3] for the values for the concentration of chloride that we obtained were not roughly equivalent to the values for the concentration of base in the blood, but, on the other hand, were approximately equivalent to the values for the concentration of chloride in normal plasma; nor did they ever rise to any extent above the level of the latter. It must be recalled that their work was done on dogs, with diets rich and poor in protein. The similarity between the concentration of chloride that we found in gastric contents and the concentration of chloride in normal plasma is in agreement with the results of Bulger, Stroud and Heideman.[5] However, the large quantity of base that we found in infants in the presence of a large quantity of free hydrochloric acid does not agree with their hypothesis that the free hydrochloric acid is liberated by a retention of base. Our results cannot well be compared with those of Polland, Roberts and Bloomfield,[4] since they used histamine as a stimulant of gastric secretion; under such stimulation, the concentration of chloride is apparently high.

SUMMARY

Determinations of the quantity of base, chloride, free and total acidity were made on the gastric contents of six children with gastrostomies and patent esophagi; and on the gastric contents of one adult with the same conditions. Similar determinations were made on the gastric contents of fourteen fasting new-born infants.

15. Stokes, J., Jr., and Tatum, J. R.: to be published.

16. The excess of base may have been combined with mucus which was usually present in the samples analyzed.

In the group of subjects on whom gastrostomy had been performed, we made the following observations:

1. The volumes of gastric contents of the six children were approximately from one third to one half of the volume found for the adult.

2. A large majority of the determinations on the gastric contents of the children showed little, if any, free hydrochloric acid, and seldom a large amount of total acidity, whereas considerable quantities of free and total acid appeared in the normal adult.

3. The concentrations of base and chloride in the children were variable, even in the same child, and were not equivalent, except in rare instances, to the amounts in the blood plasma. However, the values for the concentration of base were, in the great majority of instances, greater than the values for concentration of chloride.

4. There was evidence in the case of the adult favoring a gastric secretion of chloride at the same concentration as that of the chloride in the plasma, with retention of base thus accounting for the presence of free acid.

The following are our observations on the group of fourteen new-born infants:

1. The volumes of gastric contents were all very small; usually between 1 and 8 cc.

2. The free hydrochloric acid ranged from 14.4 to 57 milliequivalents per liter (cubic centimeters of tenth-normal sodium hydroxide per hundred cubic centimeters); the total acidity, from 17.4 to 67 milliequivalents per liter (cubic centimeters of tenth-normal sodium hydroxide per hundred cubic centimeters).

3. The concentrations of base and chloride were comparatively uniform. The range of concentration of chloride was from 102 to 120 milliequivalents per liter, which approximates closely that of the chloride in the plasma. The range of concentration of base was from 99 to 126 milliequivalents per liter, which was far below that of the concentration of base in the plasma (150 milliequivalents).

4. Although the amounts of base chloride are almost equivalent, a large part of the chloride must be accounted for as free hydrochloric acid; much of the base must be combined with another anion, as yet undetermined.

5. Our results favor a constant secretion of chloride by the stomach at the concentration of the chloride in the plasma, but we did not find evidence in these new-born infants for the secretion of free hydrochloric acid by the retention of base.

ETIOLOGY AND SPECIFIC TREATMENT OF MEASLES*

N. S. FERRY, M.D.
DETROIT

There are two theories concerning the etiology of measles, both of which are founded on actual laboratory and clinical experiments. The theory that the disease is caused by a filtrable virus not yet identified is based on work carried out previous to 1925 by Hektoen,[1] Anderson and Goldberger,[2] Blake and Trask [3] and others. These workers undoubtedly reproduced the disease experimentally, in either the human being or the animal, from filtered blood or filtered nasopharyngeal washings obtained from patients during the early stages of the disease. None of these investigators, however, was able to isolate or to make a culture of the virus from the filtered blood or washings or from the animal into which these body fluids or washings had been injected.

The other theory, constructed from the work reported later by Tunnicliff,[4] Ferry and Fisher,[5] Hibbard and Duval [6] and Cary and Day,[7] is that the disease is caused by an organism which can be cultivated and identified by the usual laboratory methods and which, in some stage of its life cycle, is filtrable. During the course of their studies, these workers isolated and identified from the blood or nasopharyngeal washings of patients with measles certain micrococci, apparently not all identical, of diplococcoid and streptococcoid forms. From their behavior certain laboratory and clinical tests made by their individual discoverers, these organisms seemed to be specific to the disease. Some

* Submitted for publication, Oct. 3, 1928.

* Read at the 108th Annual Meeting, Michigan State Medical Society, Detroit, Sept. 27, 1928.

* From the Medical Research Laboratories, Parke, Davis and Company, Detroit.

1. Hektoen, L.: Experimental Measles, J. Infect. Dis. **2**:238 (March) 1905.

2. Anderson, J. F., and Goldberger, J.: Experimental Measles in the Monkey, Pub. Health Rep. **26**:847 and 887 (June 9-16) 1911.

3. Blake, F. G., and Trask, J. D.: Susceptibility of Monkeys to the Virus of Measles, J. Exper. Med. **33**:385 and 413 (March) 1921.

4. Tunnicliff, R.: The Cultivation of a Micrococcus from Blood in Pre-Eruptive and Eruptive Stages of Measles, J. A. M. A. **68**:1028 (April 7) 1917.

5. Ferry, N. S., and Fisher, L. W.: Measles Toxin: Its Preparation and Application as a Skin Test, as an Immunizing Agent, and for the Preparation of an Antitoxin, J. A. M. A. **86**:932 (March 27) 1926.

6. Hibbard, R. J., and Duval, C. W.: Studies upon the Virus of Measles, Proc. Soc. Exper. Biol. & Med. **23**:853 (May 12) 1926.

7. Cary, W. E., and Day, T. A.: The Etiology of Measles, J. A. M. A. **89**: 1206 (Oct. 8) 1927.

of them were shown to be filtrable, and others were said to be obtained from filtered blood taken from patients with measles and also from animals into which this blood had been injected.

There is no doubt in the minds of the majority of investigators that the primary etiologic factor of the disease can pass through the ordinary bacteria-proof filter, and that the virus or organism in its ultramicroscopic stage can produce the disease is not questioned.

It is essential, therefore, that whatever organism is advanced as the cause of the disease and finally recognized as such shall be able, ultimately, to fulfil these premises.

The severe epidemic of measles in Detroit in 1926 afforded Mr. Fisher and me the opportunity to study the disease thoroughly from a bacteriologic standpoint. From the blood taken during the early stages of the disease a streptococcus of the viridans variety was isolated in pure culture. In many laboratory tests and animal inoculations, the organism seemed to give undoubted evidence of specificity. This work, which was first reported in *The Journal of the American Medical Association*,[5] was carried out through the courtesy and with the assistance of the Detroit Board of Health and with the direct aid of members of the Herman Kiefer Hospital, Detroit.

The apparent specificity of the organism, called *Streptococcus morbilli*, is partially confirmed by the facts that were published in the earlier paper; further evidence of a more significant nature which appeared in later publications is herein reviewed.

The early observations which led to the conclusion that this organism might be specific to measles are as follows: The organism was isolated in pure culture from the blood taken during the early stages of the disease from several patients with extremely severe cases. When grown in liquid mediums, the organism produced a soluble or extracellular toxin which, when injected into animals, stimulated the formation of an antitoxin; this toxin, also, when injected intradermally into the human being, in a significant percentage of cases produced positive local skin reactions in persons without a history of measles and negative reactions in persons with this history. The toxin was neutralized by diluted serum taken from patients convalescing from measles, as well as by its homologous antitoxin; it was possible thus to use either one of these neutral mixtures instead of heated toxin as a control for the toxin when making skin tests of the human being. The organism or its toxin, when injected subcutaneously or intracutaneously into albino rabbits, produced severe local reactions and generalized rashes, accompanied frequently with a characteristic hyperemia of the conjunctivae suggestive of measles in the human being. These reactions could be prevented by neutralizing the toxin with measles antitoxin or with serum from patients convalescing from measles, or by previous injection of either of these serums into the

animals; persons reacting positively to the toxin gave negative reactions after subcutaneous injections of either serum from patients convalescing from measles or of measles antitoxin.

Since none of these reactions, attributed to the extracellular or soluble toxin of the organism, had been produced previously with any organism isolated from subjects with measles, they were assumed to be characteristic. Because of the consistent appearance of these reactions and their relation to previous results with other soluble toxins, it was reasoned also that they must indicate the specific nature of the organism.

Further work on the organism, therefore was carried out by Ferry and Noble,[8] and other evidence of a more or less positive nature was produced which revealed some interesting and apparently important facts concerning the specificity of the so-called "measles streptococcus." The study of eighty-three consecutive cases showed that the serum from patients convalescing from measles agglutinates *S. morbilli,* in fairly high dilution, in 86.7 per cent of the cases as compared with 9 per cent for other micrococci considered specific to measles.

Furthermore, morphologic, cultural and serologic reactions showed that the various micrococci producing green pigment and described by several authors as probable causes of measles, are not all alike. The conclusion followed that if all of these various organisms were the cause of measles they must belong, somewhat like the pneumococcus, to a heterogeneous group composed of several distinct types.

Another recent paper, a collaboration by Ferry, Gordon, Munro, Steele and Fischer,[9] contained a report of clinical experiments with measles toxin and antitoxin carried on during 1928 at the Herman Kiefer Hospital and the Children's Hospital, Detroit, the Children's Convalescent Home, Farmington, and the Wayne County Training School, Northville.

The results with this antitoxin were not comparable to those obtainable with some of the older antitoxins, such as those for diphtheria and tetanus; nevertheless, they gave evidence of the protective value of the serum, and further indicated the specific nature of the toxin and its antitoxin. The paramount question was, "will the antitoxin, in a thoroughly controlled series of cases, actually protect exposed susceptible children against authentic cases of measles?" An affirmative answer would, of course, strengthen the theory as to the place of measles streptococcus in the etiology of measles.

At the Herman Kiefer Hospital, under Dr. Gordon, 250 children who did not give a history of measles were under observation. Thirty-eight of

8. Ferry, N. S., and Noble, A.: Cultural and Serological Reactions with Green Producing Micrococci, Arch. Int. Med. **43**:274 (Feb.) 1929.

9. Ferry, N. S.; Gordon, E. J.; Munro, F. W.; Steele, A. H., and Fisher, L. W.: Clinical Results with Measles Streptococcus Toxin and Antitoxin, J. A. M. A. **91**:1277 (Oct. 27) 1928.

these patients were given prophylactic injections of 10 cc. measles antitoxin, and seven of the patients (20 per cent) contracted the disease. Eighty-five patients received prophylactic injections of 5 cc. of serum from patients convalescing from measles, and twenty-two (25.8 per cent) contracted the disease. As a control, 127 patients did not receive serum; forty (31.5 per cent) of these developed measles. As 31.5 per cent of the untreated patients contracted the disease, this figure should be taken as the percentage of expectancy among the susceptibles. The expectancy, then, was 31.5 per cent of thirty-eight or twelve, and five of twelve patients (42 per cent) were actually protected. Computed in the same way, the actual protection with serum from patients convalescing from measles at the Herman Kiefer Hospital was 19 per cent.

Fifty-two patients with negative histories for measles were under observation at the Children's Hospital, under Dr. Munro. Twenty-six of these patients were given injections of 20 cc. of measles antitoxin and one (3.8 per cent) contracted the disease; eight (30.7 per cent) of the twenty-six untreated patients, contracted the disease. With the figure 30.7 per cent to determine the expectancy, it was computed that 88 per cent were actually protected. The higher percentage of protection in this institution as compared with that in the Herman Kiefer Hospital could probably be accounted for by the fact that a larger dose of antitoxin was given.

At the Children's Convalescent Home, under the direction of Dr. Munro, susceptibility to measles was determined according to susceptibility to the skin test dose of measles toxin instead of according to the histories. In the infant ward, a small ward where all children had been well exposed to the disease, six patients giving positive reactions received 20 cc. of antitoxin, and six were left untreated as controls. One (16.6 per cent) of the treated patients who already was suffering with the disease developed a rash on the fourth day; three (50 per cent) of the untreated patients contracted the disease after the usual period of incubation. The expectancy in this instance was 50 per cent of the six patients or three. The actual protection, therefore, was two of three or 67 per cent.

The average actual protection at these three institutions was 66 per cent. The average protection at the two institutions in which 20 cc. of antitoxin was given was 78 per cent, as compared with 42 per cent when the dose was 10 cc. Following these injections of horse serum at the three institutions, the usual number of cases of serum sickness were reported.

All of the children at this institution were tested for susceptibility to measles with the intradermal test composed of one skin test dose of measles toxin. It is, therefore, of interest to note the number of cases of measles as compared with the result of the diagnostic skin test. Fourteen (31.8 per cent) of the forty-four patients showing positive skin

tests developed measles and five (21.7 per cent) of the twenty-three who gave pseudoreactions developed the disease. Only nine (9 per cent) of the ninety-nine patients who reacted negatively developed the disease. The results of this test also point strongly toward the specificity of the measles toxin, since the number susceptible to the toxin seemed to be in about the same proportion as those susceptible to the disease.

Thirteen of the fourteen patients who reacted positively, who developed measles and who were still in the hospital ten weeks after recovery were retested, and none gave positive reactions. In other words, the development of measles and the recovery produced a sort of antitoxin in the patients which neutralized the measles toxin prepared from *S. morbilli* and caused all thirteen patients reacting positively to give negative reactions. These results also indicate strongly the specific nature of the toxin.

At the Wayne County Training School, the work was carried on under the supervision of Dr. Steele. Although none of the patients at the institution had measles at the time, some interesting tests were carried out with measles toxin, serum from patients convalescing from measles and measles streptococcus antitoxin, to compare the neutralizing value of the two serums against the toxin when used as a skin test on susceptible persons.

The test was carried out in a manner similar to the test for determining the protective value of scarlet fever antitoxin. The serums were found to neutralize the measles toxin in about equal proportion. Each serum contained, on the average, 10,000 neutralizing units; in other words, 1 cc. of either the antitoxin or the serum from patients convalescing from measles was capable of neutralizing 10,000 skin test doses of the measles toxin.

If it is proved ultimately that the streptococcus toxin is specific to measles, the results of this test may reveal the reason that the results following the use of serum from patients convalescing from measles were less favorable at the Herman Kiefer Hospital than were those from measles antitoxin. The dose of measles antitoxin, which had an equal number of neutralizing units, was twice that of the serum from patients convalescing from measles, a fact which undoubtedly gave it greater protective value.

I wish to report at this time, also, the results of an experiment which was carried out in 1926 by Dr. E. Martmer of Detroit on fifty-one infants, all less than 3 months of age, at the Florence Crittenden Home. This experiment turned out to be of more than passing interest, as affecting the question of the conveyance of passive immunity to infectious diseases from mother to nursing child through the mother's milk.

These fifty-one children all were tested for susceptibility to measles toxin with one skin test dose of toxin each. There were two controls:

In one, the toxin was neutralized with measles antitoxin obtained from the goat and in the other, with measles antitoxin obtained from the horse. These animals had been hyperimmunized previously with measles for the preparation of experimental antitoxins.

Six of the fifty-one infants responded with positive skin reactions, denoting susceptibility to the toxin and also to measles, pending the ultimate proof that this toxin was specific to measles. As children less than 6 months of age are, as a rule, immune to measles, the histories of the six cases were examined for an explanation of this reaction. It was found that the mothers of the children had aborted, and that all the infants were being fed on cow's milk. I do not know how many of the forty-five infants giving negative reactions were also bottle-fed; the percentage, however, was small as compared with those giving positive reactions.

While this experiment does not prove, it strongly suggests a relationship between mother's milk and immunity in the nursing infant and corroborates similar experiments previously reported by Ehrlich,[10] Famulener,[11] Theobald Smith [12] and others.

Another interesting outcome of this experiment has a bearing on the question of the relative susceptibility of infants to horse serum and goat serum.

It was found that fourteen (28 per cent) of the infants were sensitive to goat serum, as shown by the skin reactions of the control mixtures, and that nine (18 per cent) were sensitive to horse serum. It would appear from these results that more children are sensitive to goat serum than the literature seems to show, and doubt arises as to the advisability of goat serum instead of horse serum when large amounts are to be given. This substitution has been advocated recently in an endeavor to lower the incidence of serum sickness which follows the use of therapeutic antiserums in a certain percentage of cases. Goat serum, however, seems to have an advantage over horse serum only when used as a neutralizing agent in diphtheria toxin-antitoxin mixtures.

SUMMARY AND CONCLUSION

An earlier group of investigators proved that the virus of measles could be passed through a supposedly bacteria-proof filter and made to produce the disease experimentally in animals and in man.

Another group of investigators, working more recently and independently, demonstrated that certain micrococci, which could easily be

10. Ehrlich, P.: Ueber Immunität durch Vererbung und Säugung, Ztschr. f. Hyg. u. Infectionskrankh. **12**:183, 1892.

11. Famulener, L. W.: On the Transmission of Immunity from Mother to Offspring, J. Infect. Dis. **10**:332 (May) 1912.

12. Smith, T.: The Significance of Colostrum to the New-Born Calf, J. Exper. Med. **36**:181 (Aug.) 1922.

cultivated and identified, gave more or less positive evidence of being specific to the disease.

On the surface, it would appear that these two claims, based on apparently different theories, are diametrically opposed; one assuming the presence of a filtrable virus, the other dealing with an organism apparently too large to filter.

Experiments with filtration, carried out by Hibbard and Duval and Tunnicliff on one of the organisms in question, and by other investigators on other apparently mutable organisms, would seem to justify entirely the assumption that these streptococci, in some stage of their life cycle, especially when developing in the blood or tissues of their host, are capable of penetrating the filters. It is justifiable to assume also that these organisms, in the filtrable stage, can produce the disease and still not be cultivable on mediums similar to that used when the original experiments were carried out.

Later evidence is reviewed to strengthen the theory of the specific nature of this organism. In a series of eighty-three consecutive cases, serum from patients convalescing from measles agglutinated the *S. morbilli* in 86.7 per cent, as compared with the 9 per cent reported for certain other micrococci considered specific to the disease. If the agglutination test indicates anything of a diagnostic nature, these results should be considered of extreme importance in the etiology of the disease.

It was also shown that an antitoxin, prepared by immunizing horses with the measles streptococcus toxin, appeared to protect susceptible persons, when used prophylactically in sufficiently large doses, and when controlled at the same time with an equal number of untreated patients under the same conditions and in the same wards.

Considered in the light of results secured in the skin test with other soluble toxins of a specific nature, the facts that the measles toxin is neutralized by diluted serum from patients convalescing from measles, that a positive reaction with the toxin becomes negative following an attack of measles and that the antitoxin gives strong evidence of protection against measles, seems to warrant serious consideration of the specific relationship of the streptococcus to measles and to justify further study of this problem from both an experimental and a clinical standpoint.

Case Reports

CONGENITAL HEART BLOCK

WITH REPORT OF A CASE *

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Finding an infant with a congenital heart lesion is always an interesting event in a children's clinic. The presence of a dissociation between the upper and lower chambers of the heart makes it doubly so, especially when this is accompanied by tachycardia and apparent arrhythmia, as any derangement in the youthful conducting system is rare in comparison with that of the adult heart with its past possibilities and tendency to scleroses and degenerations.

Up to the time this paper was written (June, 1928), twenty-one graphically proved cases of congenital heart block have been reported in the literature. These are represented in the accompanying table under their most prominent features which show some resemblance in the age of the patients, the clinical diagnosis of ventricular septal defect, the bradycardia, the usual lack of symptoms and the frequency of the change in the grade of block present.

A congenital defect in the formation of the heart which interferes with its conducting system appears to be the most common cause of permanent heart block in the child. The dissociation which is occasionally found in acute infection, rheumatism, asphyxia and overdigitalization is usually transient; in the congenital type the condition is permanent, although the grade of block may vary according to existing conditions, an increase in auricular rate usually being followed by an increase in the degree of block present.

In her article on congenital defect of the heart, Maude E. Abbott [1] gives as the etiology: (*a*) arrest of growth at an early stage—due not

* Submitted for publication, Sept. 21, 1928.

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1. Abbott, M. E.: Congenital Heart Disease, in Osler: Modern Medicine, Philadelphia, Lea & Febiger, 1927, vol. 4, p. 612.

so much to a hereditary predisposition as to a diseased condition of the fetal envelopes or maternal tissues (rheumatism, tuberculosis, syphilis); (*b*) fetal disease, which plays a minor rôle but is found especially when valvular stenoses and atresias are present (rheumatism, syphilis).

Heredity probably is a factor in the etiology as far as the condition is considered a congenital defect, but the cardiac lesion itself commonly precludes propagation of its kind.

In the postmortem examinations made on hearts which demonstrated high grade block during life, lesions affecting either the auriculoventricular node or the bundle have usually been found,[2] an illustrative example being the instance reported by Armstrong and Mönckeberg[3] in a 5 year old child with heart block, whose heart at postmortem showed a small tumor localized in the auriculoventricular node.

Wilson and Grant[4] have recently described a condition in a child of 14 months, in whom the ventricular septum was absent and the conducting system followed an abnormal course from a well developed auriculoventricular node in the interauricular septum near the coronary sinus. They found a muscular prominence on the postventricular wall commencing at the interauricular septum, behind the aortic orifice, lying between the mitral and tricuspid valves and breaking into trabeculae toward the apex. This prominence is regarded by them and others[5] as the rudiment of the posterior horn of the interventricular septum. Wilson and Grant found that in their case two main strands of nodal tissue accompanied by blood vessels passed through dense fibrous tissue from the auriculoventricular node to this muscular prominence where they seemed to appear as a single narrow band penetrated and surrounded by fibrous tissue. The band was followed with difficulty but seemed to spread out into definite Purkinje fibers after passing down the muscular prominence and giving off one branch to the right anterior portion of the ventricle.

It is not unreasonable to believe that varying degrees of block could be present according to the amount of pressure exerted on the few conducting fibers by the blood vessels in their dense fibrous casing, as in the instance described by Cohn, Holmes and Lewis[6] in a woman in whom the block was spasmodic and in whom at necropsy the fibers of the auriculoventricular bundle were widely separated by large venous

2. Lewis, T.: Mechanism of the Heart Beat, London, 1911, p. 100.

3. Armstrong, H., and Mönckeberg, J. G.: Herzblock, bedingt durch primären Hertztumor, bei einem 5-jahrigen Kinde, Deutches Arch. f. klin. Med. **102**:144, 1911.

4. Wilson, J. G., and Grant, R. T.: Heart **12**:295 (March) 1926.

5. Mönckeberg, J. G.: Stud. z. Path. d. Entwcklng. **11**:448, 1920.

6. Cohn, A. E.; Holmes, G. M., and Lewis, T.: Heart **11**:241, 1910.

Author	References	Sex	Age Proved	Slow Pulse Noted	Congenital Malformation	Cardiac Enlargement	Grade of Auriculo-ventricular Block	Ventricular Rate	Syncopal Attacks	Observations
Van der Heuvel, G. C. T.	Proefschr. aan de Rijks Univers. Groeningen, 1908	F	23 yr.	15 yr.	Interventricular septal defect	Marked	Complete	34	Present first at age of 2 years	Slight cyanosis
Fulton, Z. M. K.: Judson, C. F., and Norris, G. W.	Am. J. M. Sc. **140**: 339, 1910	M	22 mo.	7 days	Interventricular septal defect	Slight	Complete	42-50	None	
D'Espine, A. J. and Mlle. Cottin	Bull. Acad. de med., Paris **74**: 202,1915	M	8 yr.	8 yr.	?	Slight	Complete	20-32	Once	
Whipham, T. R.	Brit. J. Child. Dis. **12**: 321, 1915	F	18 mo.	18 mo.	Interventricular septal defect	Slight	Partial 2:1	56-64	None	
Whipham, T. R.	Brit. J. Child. Dis. **12**: 321, 1915	F	12 yr.	6 yr.	Interventricular septal defect	Marked to left	Complete and 3:2, 2:1, etc.	40-64	None	
Bass, M. H.	J. A. M. A. **70**: 287 (Feb. 2) 1918	M	15 yr.	13 yr.	?	Slight	2:1 and complete	37	None	
Gorter, E.	Nederl. Maandschr. v. Verlosk., 1919	M	6 mo.	6 hr.	?	?	Complete	72	None	Slight cyanosis
Rosenson, William	Arch Pediat. **37**: 103, 1920	F	10 yr.	8 yr.	Communication between aorta and pulmonary artery just above aortic valve ?	Marked	Complete and partial	44	None	
Carter, E. P., and Howland, J.	Bull. Johns Hopkins Hosp. **31**: 351, 1920	F	3 yr.	3 yr.	Interventricular septal defect	Slight	Complete	37	Once at 4 years of age	
Smith, S. C.	J. A. M. A. **76**: 17 (Jan. 1) 1921	M	20 yr.	20 yr.	?	Slight	Complete	43	Present first at 3 years	
White, P. D.; Eustis, R. S., and Kerr W. J.	Am. J. Dis. Child. **22**: 299 (Sept.) 1921	F	4 days	4 hr. before birth	Interventricular septal defect	Marked	Partial 2:1 and less	70	.....	Mongolian idiocy; right preponderance (marked) by electrocardiogram; slight cyanosis
White, P. D.; Eustis, R. S., and Kerr, W. J.	Am. J. Dis. Child. **22**: 299 (Sept.) 1921	M	6 yr.	5½ yr.	?	Moderate	Complete	46	.....	Slight cyanosis on exertion

Barbier, Lebec and Mouquin	Soc. de pediat., Arch. d. mal de coeur **15:** 171 (March) 1922	F	15 yr.	15 yr.	Interventricular communication	?	Complete	44	Ocular compression caused arrest of heart with loss of consciousness	Some ventricular extrasystoles; administration of amyl nitrite caused acceleration of ventricular rhythm
J. By Frias	Arch. españ. de pediat **6:** 449 (Aug.) 1922	F	5 yr. 4 mo.	5 yr. 4 mo.	?	Slight	Complete	50	Present	Epileptiform attacks
Romberg, Eli C., and White, Paul D.	Boston M. & S. J. **190:** 591 (April 3) 1924	F	9 mo.	9 mo.	Interventricular septal defect	None	Complete	70	None	Perspiration and cyanosis
Meyer, D. P. (quoted by Vaquez: Diseases of the Heart, Philadelphia, W. B. Saunders Company, 1924, p. 533)	Arch. de mal de coeur **16:** 249, 1923	F	18 yr.	?	Dextrocardia with cardiovisceral transposition; retrecessement pulmonaire with interventricular septal defect	Present	Complete	64	None	Cyanosis since birth
Wilson, J. G., and Grant, R. T.	Footnote 4	F	14 mo.	14 mo.	Congenital pulmonary stenosis with interventricular septal defect	Present	2:1 heart block	60	None	General cyanosis; autopsy report in detail
Sprague, H. B., and White, P. D.	Footnote 8	F	12 yr.	4 yr.	Interventricular septal defect	Slight to the left	May 7, 1924, partial 2:1; Dec. 3, 1924, complete; Sept. 16, 1925, complete	40-60 45 44 50	None	No cyanosis
Shapiro, M. J.	Minnesota M. J. **10:** 566 (Sept.) 1927	F	9 yr.	7 yr.	Probably pulmonary stenosis	Present	2:1	65	None	Cyanosis present; sudden death, Feb. 5, 1925; no autopsy
McIntosh, R.	Am. J. Dis. Child. **34:** 965 (Dec.) 1927	F	7 mo.	7 mo.	Probably a ventricular septal defect close to the auriculoventricular septum	Present	Complete	57	None	Died, no autopsy; atropine sulphate, 1/500 grains every 4 hours for 2 days; no effect on heart rate
Davis, J. H.	Am. J. Dis. Child. **35:** 724 (April) 1928	M	3 mo.	3 mo.	Interventricular septal defect	Present	Complete	45-56	None	No symptoms; atropine had no effect on ventricular heart rate

sinuses. They attributed the transient dissociation in the conducting system to pressure through intermittent swelling of these sinuses. Lewis said that "a rise in blood pressure in the blood vessels or lymph spaces of this region may extinguish conduction which is already precarious, by altering tissue tension."

The sequence of auricular and ventricular contraction is dependent on a clear pathway. The natural pacemaker of the heart is the sino-auricular node which is found at the junction of the superior vena cava with the right auricle. Impulses are generated in the sino-auricular node at the rate of from 101 to 134 per minute in the 12 month old child, (Vierodt), and are transmitted normally to the auriculoventricular node in less than 0.2 second, from where they are conducted along the bundle of His and its branches. If, however, an obstruction should block the impulse before it reaches the ventricle, new waves are generated by a second pacemaker, lying below the interference, and ventricular contraction continues in abeyance to this new rhythm, which is, as a rule, of a slow rate.

The auriculoventricular node, which is similar in structure and morphology to the sino-auricular node, although it has a slower rate of exciting impulses,[7] may become the ventricular pacemaker, or this may be found in the junctional tissues or in one of the main branches. The electrocardiogram shows clearly whether the impulse starts above or below the main bundle through the ventricular curve which is anomalous if infraventricular in type and normal in outline if supraventricular in origin.

In figures 2 and 4, the ventricular or Q.R.S. deflections are similar to those in a normal electrocardiogram in which the ventricle contracts to a stimulus originating above the division of the bundle. There is no widening of the Q-S interval as there would be if the origin of the stimulus were below the bundle; therefore, the impulse preceding the ventricular contraction in this case must arise in the junctional tissue and pass along the divisions of the bundle without interruption.

In the case of Wilson and Grant,[4] in which the conducting system was found to follow an abnormal course, the Q.R.S. complex was also normal in outline, showing that the impulse originated above the ventricle and also that it spread through the fibers to both sides of the combined ventricle simultaneously.

SYMPTOMS AND PROGNOSIS IN CONGENITAL HEART BLOCK

Heart block may be present in a child without any symptoms of discomfort, the condition being discovered by accident. Bradycardia is the

7. Lewis, T.: The Mechanism and Graphic Registration of the Heart Beat, London, 1925, pp. 421, 181, 183 and 347.

most constant symptom. When the anatomic lesion is complex, symptoms of cyanosis and clubbing of the fingers may be found, but this is usually due to the type of lesion present. The block itself is not a serious progressive process,[8] and the prognosis of the case depends on the efficiency of the circulation. Intercurrent infections are usually not well borne.

The Stokes-Adams syndrome is not common in younger persons with congenital heart block. Although nutrition is not necessarily impaired, its degree depends on the competence of the cardiac mechanism which varies according to the complexity of the lesion.

Sudden death occurs fairly frequently. Aldrich [9] told of a girl, aged 12 years, with a 3:1 block, who did not present any symptoms and lived a normal existence and who died suddenly while standing in the water just before starting to swim. Such death is probably due to some further interference in a defective conducting passage with resultant failure of ventricular response.

The diagnosis of congenital heart block is seldom difficult. The condition is usually discovered by the presence of bradycardia and of a loud systolic murmur heard best over the midprecordium, but neither the bradycardia nor the murmur are pathognomonic and either or both are occasionally absent, as in the instance reported later on in this paper in which a rapid pulse rate was constant even when the electrocardiogram showed a complete auriculoventricular dissociation. Lewis [7] explained a high ventricular rate in complete block as one in which the obstruction occurs high in the auriculoventricular node itself.

When marked bradycardia is present the auricular contractions are sometimes audible,[7] but the graphic methods alone eliminate the possibility of error and determine the diagnosis. In the electrocardiogram are seen the regular summits of the P waves or auricular contractions falling without relationship to the Q.R.S. or ventricular deflections which also are found to be contracting regularly but usually at a slower rate than that of the auricles. When dissociation is of a high grade but not complete the ventricular deflections bear a definite relationship to the auricular contractions, responding to every second, third, fourth, or other, impulse received or alternating a 2:1 with a 1:1 or a 3:1, or other, response. High grades of block are common in congenital dissociation. In the lowest grades of obstruction the ventricle responds to each auricular stimulus, but the passage of the excitation wave from auricle to ventricle is retarded so that the P-R interval exceeds 0.2 second in time.

8. Sprague, H., and White, P.: M. Clin. N. Amer. **10**:1235 (March) 1927.

9. Aldrich, C. A.: Discussion, Tr. Chicago Ped. Soc., June 6, 1927.

In the cases reported in which several electrocardiograms were taken it was commonly found that complete block alternated with high grade blocks on different dates. Possibly this variance would be more common if tracings were repeated more frequently. Theoretically, in those cases in which absolute anatomic dissociation was not present, the block would vary according to the tissue tension exerted on the strands lying in abnormal positions, so that it could spasmodically become complete or partial, determined by the increase or relief of pressure in the surrounding tissues.

As an illustration of this variance in degree of block, an additional case of congenital cardiac dissociation is presented.

REPORT OF CASE

History.—Guson G., a boy, aged 12 months, of Jewish parentage, was admitted into the wards of the Children's Medical Division of Bellevue Hospital on Nov. 11, 1927, with a diagnosis of congenital heart disease with arrhythmia. The

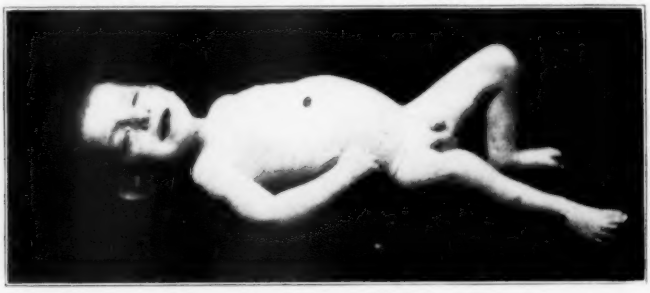

Fig. 1.—Appearance of patient at age of 12 months.

family history was unimportant, and the mother did not know of any case of congenital anomaly in the family. The father, mother and sister were alive and well. The delivery, which occurred at term, was normal; the child weighed 7½ pounds (3,401.9 Gm.), cried lustily and was not cyanotic. He was circumcised on the eighth day. He was weaned at the age of 6 weeks and was given a modified whole milk feeding. His early months were uneventful. He slept well, although he suffered occasional colds and was underweight. He gave little trouble and seemed well and happy.

At the age of 5 months he began to have fits of coughing, during which he became cyanotic and exhausted and perspired freely. His eyes rolled back, and the extremities became cold and clammy. These attacks occurred from three to four times a day and were often checked by immersing the body in warm water and tapping the plantar surface of the feet. Vomiting occurred almost immediately after the coughing spell. This condition continued for two months and was probably pertussis.

The patient began to sleep poorly and cry a good deal; he was constipated and did not gain well. He was still on modified whole milk feeding. Cod liver oil, vegetables and cereals had not been added to his diet at any time.

Examination.—On admission, the child was poorly developed and nourished, weighing 13 pounds 10 ounces (6,180 Gm.) (fig. 1). Temperature and respiration were normal. The patient was unable to talk or sit up alone and was fretful and cried constantly.

Head: The hair was scanty. The frontal and parietal bosses were prominent, as also were the veins of the scalp. The anterior fontanel admitted two finger tips. The skin was rough and dry. The eyes, ears and nose were normal. Two central upper incisor teeth were present. The mucous membrane of the mouth was pale and did not bleed on pressure. The tongue, pharynx, palate and tonsils were normal. The neck did not show adenopathy or visible venous pulsation.

Chest: The chest showed a moderate rosary and Harrison's groove. The lungs were normal on percussion and auscultation.

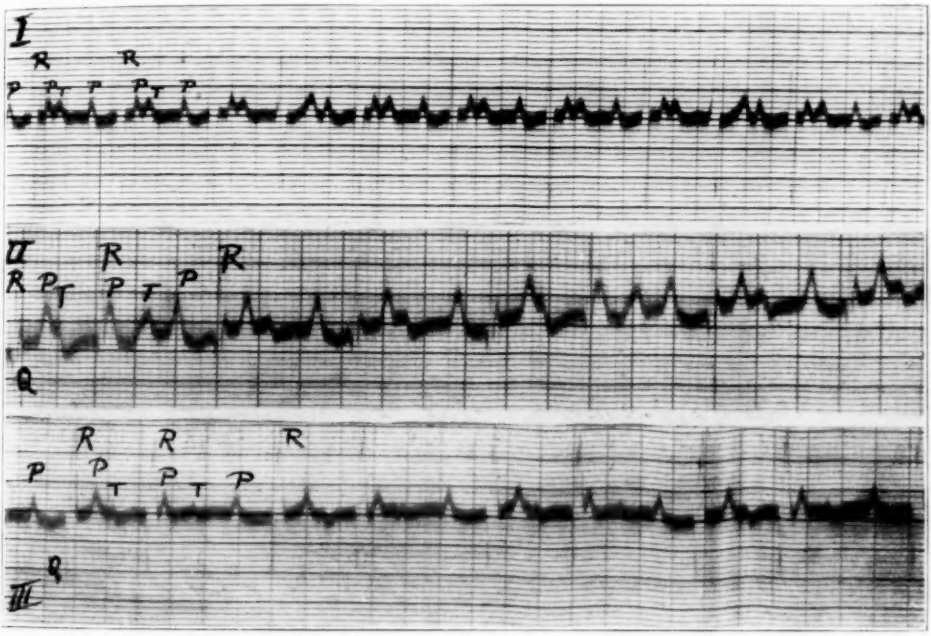

Fig. 2.—Electrocardiogram composed of lead 1, lead 2 and lead 3, each taken on a different date in November, 1927, and each showing a different degree of block (described in text).

Heart: On inspection, an irregular wavy impulse could be seen passing over the second to the fifth left intercostal space. There was an epigastric pulsation below the xiphoid. Palpation showed a systolic thrill over the same areas, maximum in the fifth intercostal space, 5.5 cm. from the midsternal line. The left border of cardiac dulness was elicited 5 cm. from midsternum in the second intercostal space; 6 cm. in the third space; 5.75 cm. in the fourth space, and 5.5 cm. in the fifth space. The right border was 1.5 cm. to the right of the midsternum, in the third interspace. A loud musical systolic murmur was heard over the entire heart, loudest over the third left interspace. The murmur was also clearly audible posteriorly, especially over the lower left scapula. The heart sounds were of fair quality, and of rapid rate, and occasionally a rhythmic arrhythmia was noted.

The irregularity appeared frequently, and was diagnosed clinically as runs of coupled beats intercepting a simple tachycardia.

Abdomen: The abdomen was tense, the spleen was not palpable and the liver was felt 2 cm. below the costal margin in the midclavicular line.

Extremities: The extremities were cold and somewhat cyanosed; the epiphyses were enlarged. The reflexes were normal.

Laboratory Examination.—The blood count showed 5,800,000 red cells, with 70 per cent hemoglobin (Sahli) and 16,650 leukocytes with 38 per cent polymorphonuclears. Achromia was present. The blood chemistry was normal. The urinalysis was negative. The Wassermann, Shick and Mantoux reactions were all negative.

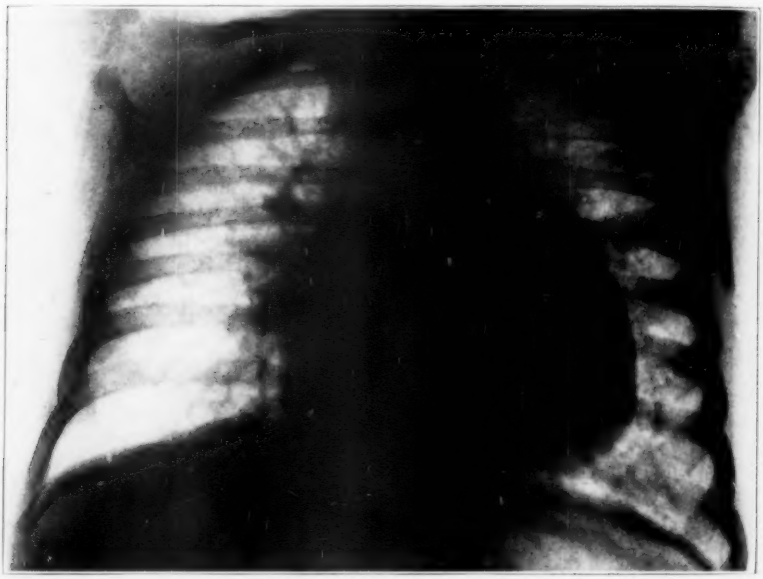

Fig. 3.—Roentgenographic appearance of heart; distance of tube, 6 feet.

Several electrocardiographic records taken at different intervals in November and December showed a dissociation betwen the auricles and ventricles. The condition varied between a complete (lead 2, fig. 2) and partial block. The incomplete dissociation also differed in the degree of ventricular response found, giving the following grades: a 2:1 block (lead 1, fig. 2) with an auricular rate of 184 and a ventricular rate of 92, and a 2:1 block alternating with a 1:1 (lead 3, fig. 2) with an auricular rate of 156, and a ventricular rate of 104 and higher degrees on other occasions.

During a period of arrhythmia similar to that diagnosed on admission as coupled beats, the electrocardiogram showed a 2:1 alternating with a 1:1 block. The auricular rates varied between 156 and 184, and the ventricular between 80 and 105 per minute.

A roentgenogram of the heart showed it to be of globular outline and enlarged to the right and left (fig. 3). Pathologic changes were not present in the long bones.

Subsequent Course in the Hospital.—The patient had three slight short febrile periods during his seven weeks in the hospital. They were all associated with bronchitis. At no time did he manifest any cyanosis, coughing or vomiting, as described earlier in the history. Occasionally, during examination, he would hold his breath and cry, becoming slightly cyanosed until he breathed, but this was considered an act of temper. His pulse was not affected. He perspired freely, and his body became covered with a sudaminal rash which caused considerable discomfort and scratching. Constipation was a constant symptom. In afebrile periods he seemed happy and contented.

The pulse rate, which was taken at different times during the day and night and following varying degrees of body activity, was found to vary from 88 to 96.

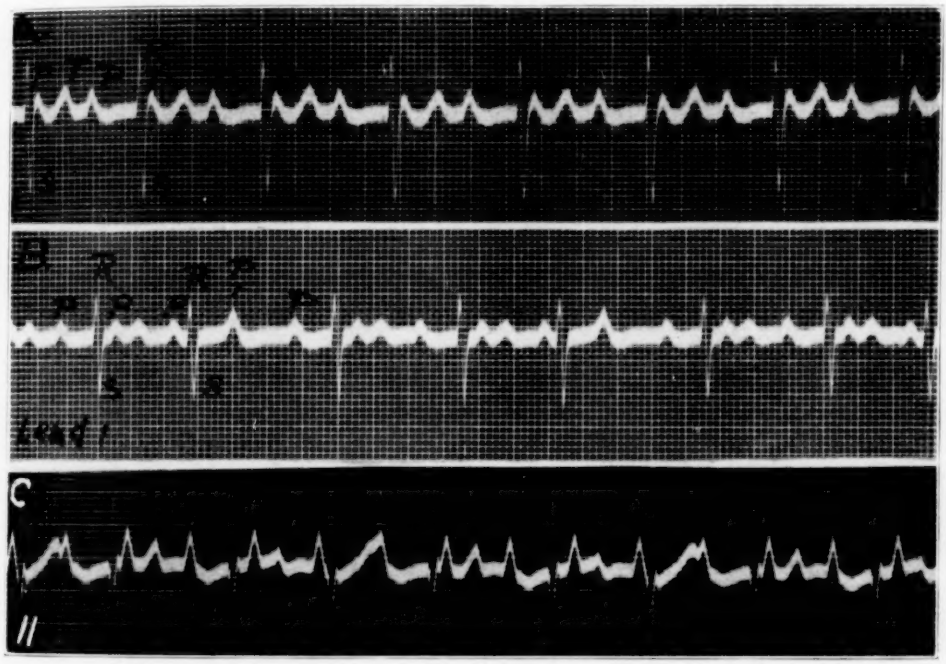

Fig. 4.—*A*, record of lead 1, June 21, 1928, showing 2:1 block with regular ventricular rate of 78 per minute; *B*, lead 1, June 27, 1928, illustrated phase of 2:1 block in which every third ventricular contraction is preceded by a short P-R interval giving a regular arrhythmia to the pulse with a rate of 85. The auricles are contracting regularly at 170 per minute.

C shows a 2:1, 2:1, 1:1 block in lead 2, June, 1928. P is superimposed on T in every third cycle.

Atropine, $\frac{1}{400}$ grain was given hypodermically and had no effect on the pulse rate or electrocardiographic record.

The patient was discharged on Dec. 28, 1927, after being in the hospital for forty-eight days, during which time he showed a loss of 6 ounces (170 Gm.). When this paper was written, he was attending the outpatient department where he was gaining weight slowly on a general diet and on cod liver oil.

COMMENT

An instance of congenital cardiac defect with peculiarities of pulse rate and rhythm is presented. The electrocardiogram shows the arrhythmia to be due to a defect in cardiac mechanism which varies in its action. In this type of lesion of the heart, high grades of heart block are seen frequently to alternate with complete dissociation. The theory that this change is due to variance in tissue tension around the defective conducting fibers is suggested.

CONGENITAL ATRESIA OF THE INTESTINE*

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BOSTON

Although rare, congenital atresia of the intestine occurs with sufficient frequency to be of clinical importance. Calder [1] first called attention to this condition in 1733, and case reports, discussions of etiology, symptomatology and treatment have appeared at intervals since, more frequently during the past quarter century. Attention should be called particularly to the comprehensive discussion of Spriggs [2] in 1912. He reported twenty-four cases and tabulated 328 others which he found in the literature to that date. In 1922, Davis and Poynter [3] tabulated about 400 cases which they found in the literature, and discussed their etiology and symptomatology. In the same year, Quinland [4] reported seven cases from this clinic and the Warren Anatomical Museum of the Harvard Medical School, together with twenty cases of imperforate anus. During the past six years, case reports have been published by Shea,[5] Sweet and Robertson,[6] Weeks and Delprat,[7] Croskery,[8] Parmelee and Miller,[9] Loitman,[10] Naegeli,[11] Brachetto-Brian and Bettinotti,[12] Sheldon,[13] Erb,[14] Farr and Fries,[15] Farr and Brunkow,[16] Dearth,[17] Hueter,[18] Hellsten and Holmdah [19] and Braeunig.[20]

* Submitted for publication, Aug. 6, 1928.

* From the Infants' and Children's Hospitals and the Departments of Pathology and Pediatrics, the Harvard Medical School.

1. Calder, J.: Medical Essays, Edinburgh, 1733.
2. Spriggs, N. I.: Guy's Hosp. Rep. **66**:143, 1912.
3. Davis, D. L., and Poynter, C. W.: Surg. Gynec. Obst. **34**:35, 1922.
4. Quinland, W. S.: Boston M. & S. J. **187**:870 (Dec. 14) 1922.
5. Shea, B.: Brit. M. J. **2**:549 (Sept. 24) 1927.
6. Sweet, G. B., and Robertson, C.: Arch. Dis. Child. **2**:186 (June) 1927.
7. Weeks, A., and Delprat, G. D.: S. Clin. N. Amer. **7**:1193 (Oct.) 1927.
8. Croskery, S. E.: Brit. M. J. **2**:787 (Oct. 29) 1927.
9. Parmelee, A. H., and Miller, E. M.: S. Clin. N. Amer. **7**:649 (June) 1927.
10. Loitman, C.: Boston M. & S. J. **197**:21 (July 7) 1927.
11. Naegeli, T.: Ztschr. f. Geburtsh. u. Gynäk. **91**:635, 1927.
12. Brachetto-Brian, D., and Bettinotti, S. I.: Semana méd. **2**:1740 (Dec. 22) 1927.
13. Sheldon, W. P. H.: Arch. Dis. Child. **1**:279 (Oct.) 1926.
14. Erb, I. H.: Am. J. Path. **2**:137, 1926.
15. Farr, C. E., and Fries, M.: S. Clin. N. Amer. **5**:621, 1925.
16. Farr, R. E., and Brunkow, C. W.: Arch. Surg. **11**:417 (Sept.) 1925.
17. Dearth, W. A.: Atlantic M. J. **27**:226 (Jan.) 1924.
18. Hueter, C.: Jahrb. f. Kinderh. **106**:245 (July) 1924.
19. Hellsten, O. T., and Holmdah, D. E.: Hygeia **85**:833 (Oct. 31) 1923.
20. Braeunig, K.: Deutsche Ztschr. f. Chir. **176**:227, 1922; Abstr., J. A. M. A. 80:967 (March 31) 1923.

Thorndike [21] recently published a report of six cases of congenital stenosis and atresia of the duodenum, with a discussion of atresia of this portion of the bowel.

The necropsy observation of an atresia of the terminal jejunum in an infant brought to the hospital with the history of persistent vomiting since birth has called my attention to this type of congenital abnormality. In the clinical and pathologic records of the Infants' and Children's Hospitals for the past fifteen years, there are thirteen instances of complete and three of partial atresia of the intestines. Quinland [4] and Thorndike [21] each reported two of these cases. Cases of congenital hypertrophic stenosis of the pylorus, imperforate anus, and intestinal obstruction resulting from congenital anomalies of the mesentery, constricting bands, etc., are not included in this report.

REPORT OF CASE

E. C., a girl, aged 2 days, admitted to the hospital on April 23, 1928, with an irrelevant family history, was born from six to eight weeks prematurely by spontaneous delivery. Nothing abnormal was noted at birth. She was fed breast milk, three parts to one of 5 per cent lactose, 1 ounce every three hours. Shortly after each feeding, she vomited a small amount. One small bowel movement, the character of which could not be ascertained, was passed the day after birth. Enlargement of the abdomen was noticed the morning of entry.

On admission, the patient was extremely sick, with a temperature of 103 F. The abdomen was markedly distended and tympanitic. The superficial veins were engorged and the skin red. The cord was dry except for some moisture at the base. The results of the physical examination were otherwise negative. Routine laboratory procedures yielded normal results.

Nothing was passed by rectum while the patient was in the hospital, and no fecal material was obtained by enemas. The vomiting persisted; the patient became rapidly worse, and died twenty-four hours after admission. The clinical diagnoses were: prematurity, omphalitis, peritonitis.

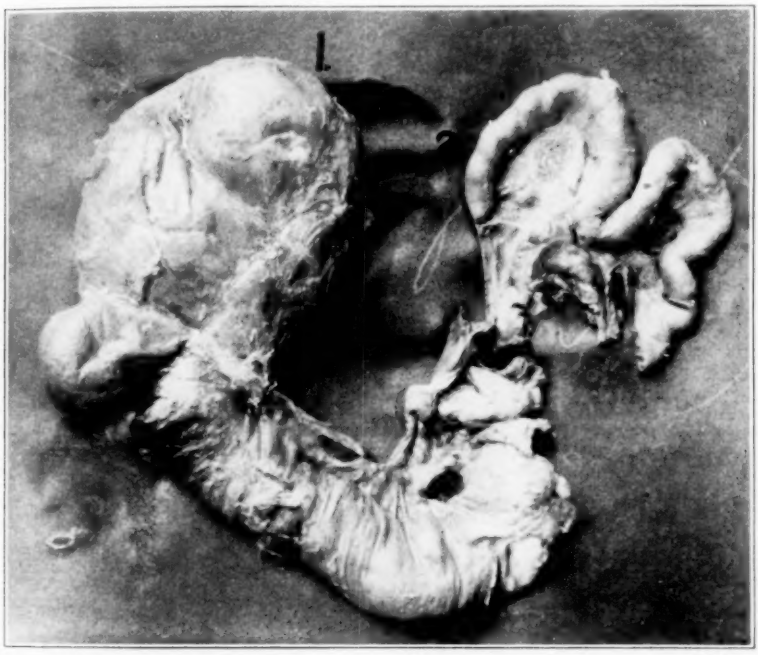
The necropsy showed the stomach and intestines in their normal positions. The stomach and duodenum were greatly distended; the jejunum was tremendously distended, ending in a large blind pouch just under the umbilicus, and its folds were matted together by thick fibrous adhesions. There was no connection between the jejunum and the lower intestines, which were contracted and contained grayish, granular material. The mesentery of the jejunum terminated with the blind end. There was a thin fibrous cord along the free margin of the mesentery of the distal blind end but not apparently attached to the intestine proximal to the atresia. Microscopic examination showed the muscle layers continuous over the blind end of the distal portion of the intestine. The mucosa of the lower intestine appeared normal (fig.). There was a fairly extensive cerebral hemorrhage, but no other observations of note were made.

The remaining eleven cases are given in tabular form (table 1).

Six of the patients presented were males and six females. The average age at entry of the patients with complete atresia was 4 days.

21. Thorndike, A.: Boston M. & S. J. **196**:763 (May 12) 1927.

The atresia was located in the duodenum and colon in one case each, in the ileum in six, and was multiple in two. Persistent vomiting and failure to pass stools were the presenting symptoms in each case. Laparotomy was done in ten of the cases. All of the patients died. Two (cases 5 and 11) lived for eighteen weeks and four weeks, respectively, after the operation and were doing well. As they began to pass small amounts by rectum, it was thought advisable to close the enterostomy stoma. Each patient died shortly after the second operation, with



Portion of the intestine of an infant, aged 2 days, showing complete atresia of the lower jejunum. *1* indicates the dilated proximal blind end; *2*, the contracted distal blind end of the intestine.

symptoms of intestinal obstruction. They might have recovered had the artificial anus been allowed to function for a longer period.

COMMENT

Persistent vomiting and absence of bowel movements in a newly born infant should always suggest the possibility of intestinal atresia. In many instances, the condition is entirely incompatible with life. If the condition is diagnosed early, however, many patients may be saved. To date, there have been four reports of cases in which relief has been obtained by operation.[6]

The etiology has not been adequately explained. Loitman [10] divided into two groups the hypotheses advanced to explain the etiology: (1) malformation or arrest in the course of normal development, including overgrowth of the epithelium to cause occlusion, occurrence at the site of an "embryological event" and anomalies in the development of the

Data in Eleven Cases of Congenital Atresia

Case	Name	Sex	Age on Admission	Duration of Life	Stools	Vomiting	Condition Found at Operation	Necropsy Observations
2	L. C.	F	4 days	6 days	0	++	None	Congenital atresia of intestine at duodenojejunal juncture
3	M. R.	F	5 days	6 days	0	++	9/5/18, colostomy; atresia of sigmoid colon	Not done
4*	T. M.	M	1½ days	3 days	0	++ Meconium	1/9/20, lateral anastomosis; excision of gangrenous blind end of ileum	Congenital atresia lower end of ileum about 3 cm. above cecum
5*	J. S.	M	4 days	19 weeks	0	++	9/13/20, enterostomy; complete atresia of ileum; 1/24/21, ileostomy, stoma closed	Partial atresia of terminal ileum and colon
6	N. L.	F	3 days	4 days	0	++	7/11/24, ileostomy	Atresia of upper ileum and rectum
7	R. V.	M	2 days	3 days	0	++	2/1/25, ileostomy; atresia of ileum	Not done
8	F. D'E.	M	10 days	10 days	0 ? Stool with enema	++	8/29/25, ileostomy; atresia of small intestine; small bowel dilated; large bowel contracted	Not done
9	A. H.	F	3 days	3 days	0	++ Meconium then bile	9/21/25, enterostomy	Atresia of midportion of ileum
10†	T. K.	M	3 days	5 days	0	++ Greenish	6/28/27, enterostomy	Multiple atresias of small intestines
11	E. Z.	F	2½ days	34 days	0	++	8/2/28, colostomy; partial atresia of colon; 8/31/18, colostomy; stoma closed; 9/1/18, exploratory laparotomy—obstructed	Not done
12	A. C.	M	1 month	34 days	Daily	++ Greenish	2/11/27, anterior gastrojejunostomy	Partial atresia of the duodenum

* In case 4, the right testis was undescended, and in case 5 there was a horseshoe kidney. There were no other remarkable necropsy observations.

† In case 10, the infant was premature by three weeks. Otherwise the past history and family history were negative in each case.

mesenteric artery and of the vitelline duct; (2) disease of the fetus, including peritonitis, volvulus, enteritis and intussusception. As there is no constant defect, one of several may be the underlying factor in a given instance.

Laparotomy is indicated immediately the diagnosis is made, the procedure depending on the operative indications. Enterostomy is most

often the method of choice; should the patient survive the initial operation, anastomosis may be done later. The enterostomy stoma should be kept open until the lower bowel is functioning normally.

SUMMARY

Twelve cases of congenital atresia of the intestine are reported.

Early recognition and operative treatment should reduce the high mortality of this relatively rare condition.

BLOOD TRANSFUSION IN ANEMIC INFANTS WITH PNEUMONIA *

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The intravenous administration of any appreciable quantity of fluid in pneumonia has usually been considered a hazardous procedure. Few have had the courage to risk a greater load on an already overtaxed myocardium and pulmonary circulation. Antipneumococcus serum in a normal saline diluent, totaling about 100 cc. per dose given to adults, has been perhaps the largest quantity of any therapeutic agent used. The transfusion of blood has received little attention in the literature and has not met with favor. Cross [1] advised intraperitoneal transfusion in bronchitis, lobar pneumonia and bronchopneumonia "where intravenous transfusions are contra-indicated." Carlton [2] concluded from his treatment of about thirty patients with bronchopneumonia and an appreciable number with lobarpneumonia that intravenous transfusion is of no benefit. He did not mention any harmful effects, however; nor did he mention the presence of anemia in any of the cases. Sir Humphrey Rolleston [3] and others did not include pneumonia as one of the diseases in which transfusion might be indicated.

Ordinarily, in pneumonia, the hemoglobin and erythrocytes are little affected. Most authorities,[4] if they consider the question at all, merely state that there is a slight reduction in the number of these cells. Maudsley,[5] in a survey of conditions of the blood in acute pneumonia, made no observations regarding the red corpuscles and hemoglobin, but confined his remarks to changes in the white cells and Arneth counts. Bass [6]

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* Submitted for publication, Sept. 12, 1928.

1. Cross, G. K.: Report on Blood Transfusion Work in the Hospital for Sick Children, Brit. J. Child. Dis. **21**:173, 1924.

2. Carlton, C. H.: Blood Transfusion in Children's Practice, Lancet **2**:850, 1926.

3. Rolleston, Sir Humphrey: Use of Blood Transfusion in Various Diseases, Brit. M. J. **2**:969, 1926. Hill, L. W.: Review of Literature on Blood and Blood Diseases of Infants and Children for Last Four Years, Am. J. Dis. Child. **25**:168 (Feb.) 1923. Hymanson, A.: Transfusion and Injection of Blood in Pediatric Practice, Arch. Pediat. **47**:440, 1925.

4. Holt: Diseases of Infancy and Childhood, New York, D. Appleton & Company, 1918. Naegeli: Blutkrankheiten und Blutdiagnostik, Lehrbuch der Klinischen Hâmatologie, Berlin, Julius Springer, 1923.

5. Maudsley, H. F.: Observations on the Blood Conditions in Acute Pneumonia, M. J. Australia **1**:484, 1921.

6. Bass, M. H.: Anemia and Pneumonia in Infants, Am. J. Dis. Child. **29**: 318 (March) 1925.

discussed the subject more at length, calling attention to Bollinger's view, expressed in 1895, that the collapse in pneumonia might be due to a practical oligemia resulting from the stasis of 30 or 40 per cent of the total volume of blood in the pneumonic area. This opinion was strengthened by the work of Leake and Brown [7] on dogs in experimental pneumonia. They found an increasing anemia as the disease progressed, with a proportionate deposition of red cells, found at autopsy, in the capillary beds in the lungs, liver and spleen. Buckman [8] corroborated this view when he concluded from a survey of infantile anemia that in acute infections the spleen may become dilated and engorged with red corpuscles, resulting in anemia of the peripheral blood. There is possibly, therefore, a relatively more pronounced anemia in pneumonia than is generally thought.

Such a condition, if not of great import in the uncomplicated case, might be of great significance in pneumonia superimposed on a preexisting anemia. In such cases, transfusion of blood may be a lifesaving measure. This treatment has received only casual mention in the literature. Morgan,[9] in Abt's "Pediatrics," for instance, states that in protracted cases of bronchopneumonia with anemia, transfusion "may confer a renewed lease on life." More recently, Buckman theoretically discussed the advisability of giving blood transfusion in any acute infection in which there is marked anemia. Although no specific statement appears in his article, the assumption is that pneumonia is included. The argument in summary is: With increase in the carbon dioxide tension, the red corpuscles swell, absorb water from the plasma and so concentrate it. This concentration is relieved by the inpouring of fluid from the tissue spaces or the gastro-intestinal tract. If, however, the hemoglobin content is too low—below 40 per cent, according to Buckman—this concentration of the plasma cannot occur; hence, the necessary transportation of water is seriously interfered with, especially in the presence of fever. Transfusion of blood is therefore advised in all cases of anemia of such degree. Bass, in 1925, was the first to emphasize this form of therapy in the acute type of pneumonia. A survey of his report of ten cases is convincing. It is true that in some of the cases the prompt fall in temperature within forty-eight hours after transfusion may have been a coincidence, since five of the patients with pneumonia treated on the fourth to the thirteenth day of the disease had one-sided cases and possibly might have had a crisis at this time without transfusion. This

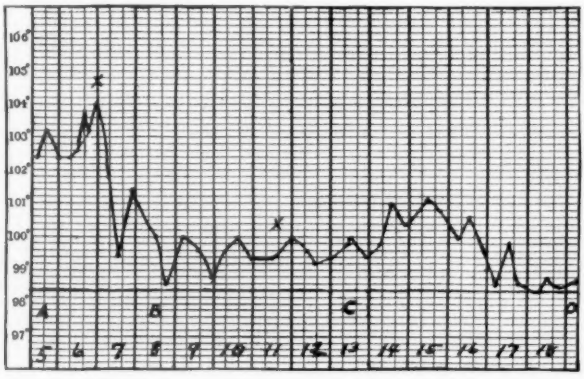
7. Leake, C. D., and Brown, T. K.: Loss of Circulatory Erythrocytes in Certain Types of Experimental Pneumonia, J. Exper. Med. **36**:661, 1922.

8. Buckman, T. E.: Observations on Anemia in Early Life, South M. J. **19**:11, 1926.

9. Morgan, quoted by Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, p. 1007.

does not explain the remaining cases, however. The point of paramount importance, moreover, is that in no case was there any harmful effect from the intravenous instillation of blood.

And yet as striking as these results were, in no instance was the anemia severe. In two cases only was the hemoglobin under 40 per cent; the lowest of these was 32 per cent. The lowest red cell count reported was 2,800,000. In a clinical study of 208 hospital cases, Lyon [10] did not mention a single case with anemia. Anemia of severe degree, however, occurs not infrequently in infants as a result of poor heredity, improper diet, rickets and poor hygienic environment. When pneumonia supervenes, the prognosis is always bad. Within the last year, two cases of this kind came under observation and prompted the publishing of this discussion; one patient died before transfusion could be attempted, while the other made an immediate and remarkable recovery following transfusion.



Variations in Temperature Accompanying Transfusion of Blood in Anemic Infant with Pneumonia

The first *x* marks the time of the first transfusion, consisting of 145 cc. of citrated blood, given at the end of the sixth day; the second *x* indicates the point at which the second transfusion, of 210 cc. of citrated blood, was made. At the point marked *A*, the blood count was 1,540,000 red blood cells (2 per cent nucleated), 25,250 white blood cells and hemoglobin 17 per cent; at *B*, the blood count was 2,540,000 red blood cells, 22,000 white blood cells and hemoglobin 25 per cent; at *C*, the red blood cells numbered 4,540,000, the white blood cells 15,000 and the hemoglobin 70 per cent; at *D*, the count was 3,830,000 red blood cells, 13,250 white blood cells and hemoglobin 50 per cent. Figures along the base of the chart indicate the days of illness.

REPORT OF A CASE

History.—A girl, aged 16 months, was breast fed for one month; thereafter she was given condensed milk only. For several months her family had noticed her pallor. She developed a cough, which persisted for six weeks, together with varying

10. Lyon, A. B.: Pneumonia in Infants and Children: A Clinical Study of 208 Hospital Cases, Boston M. & S. J. **185**:189, 1921.

degrees of fever and loss of weight. For four days she had high fever, dyspnea and harrassing cough, and refused practically all nourishment.

Examination.—With a temperature of 103 F., the patient showed severe toxemia. The pharynx was injected; the ears were normal. There were signs of frank consolidation over the entire right side of the chest posteriorly and over the left side of the chest anteriorly. Elsewhere signs of bronchitis were found. Extreme dyspnea and tympanities were noted. Urinalysis yielded negative results, and the reaction to the Pirquet test also proved negative.

Course.—The accompanying chart shows graphically the remarkable progress of the child. After receiving, very slowly, 145 cc. of citrated whole blood in the median vein, there was a prompt fall of temperature to normal in eight hours, with a proportional clinical improvement; then came a rise to 101 F. and then a return to normal. The amount of blood almost doubled. It was still low, however, and there were still signs of considerable involvement in the chest. Therefore, 210 cc. more of blood was given, this time into the left external jugular vein. There was no reaction. The red blood count jumped to 4,500,000 and the hemoglobin to 70 per cent. After four days, a slight relapse occurred with a new patch of pneumonia in the left axilla and two slight convulsions. The results of a lumbar puncture were negative, and a roentgenogram of the chest proved negative for fluid. Steady improvement followed, and the infant was discharged two weeks after the second transfusion and ten days after the pneumonic relapse. She had three times the amount of blood she had had on admission.

SUMMARY

1. Attention has been called to the bad prognosis of pneumonia in anemic infants treated without transfusion.

2. The question of transfusion of blood in such cases has been discussed.

3. A summary of a case history has been given of an infant, aged 16 months, with hemoglobin of 17 per cent and an output of 2 per cent nucleated red cells, who was treated by transfusion.

CONCLUSION

Transfusion of blood in anemic infants with pneumonia, when carefully performed, is devoid of danger and is the most valuable form of therapy available at the present time.

ENCEPHALITIS IN CHILDREN *

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CHICAGO

Encephalitis in children has become a comparatively common disease during the past ten years. Judging from the medical literature and the case records of the Children's Memorial Hospital, this is in marked contrast to its rarity before this time. Observations of children in whom such a diagnosis was made during this period seem to indicate that the increased frequency of this disorder is due largely to new or previously unrecognized clinical and pathologic syndromes which are placed under the general head of encephalitis.

Acute nonpurulent inflammation of the brain was recognized by Hayem (1867).[1] Werincke (1887)[2] described a group of cases as complications of the acute specific fevers. Strümpbell (1885)[3] suggested the name polio-encephalitis for a group of cases showing cerebral involvement and pointed out the resemblance to poliomyelitis; in 1891, he described two fatal cases of encephalitis in adults with postmortem examination. He also advanced a view that cerebral palsies of children may be dependent on an encephalitis involving the cerebral cortex. Medin (1890)[4] pointed out the cephalic component of polioencephalitis and divided the cases into three groups, cerebral, pontile and bulbar. Numerous other writers reported small groups of cases, and all indicated the comparative rarity of the disease previous to March, 1918, when the epidemic of lethargic encephalitis started in New York, the infection coming from Europe. Since 1920, however, the incidence of epidemic lethargic encephalitis has greatly decreased until at present typical cases are again comparatively rare. Nevertheless, in the wake of the epidemic the frequency of the disease continues to increase. The number of ill children having neurologic symptoms which can be interpreted only on the basis of encephalitis is apparently becoming more frequent. This frequency is illustrated by the number of cases seen at the Children's Memorial Hospital. Previous to 1918, there was a total of ten cases. During the time of the epidemic—1918 to 1920—an average of fourteen cases a year was seen. Since that

* Submitted for publication, Oct. 1, 1928.

1. Hayem, Georges: Étude sur les diverses formes d'encephalite, Paris, A. Delahaye, 1868.

2. Werincke, in Oxford Medicine, 1887, vol. 6, p. 422.

3. Strümpbell, A.: Ueber die acute Encephalitis der Kinder, Jahrb. f. Kinderh. **22**:173, 1885.

4. Medin: En epidemie of infantil paralysi, Hygiea **52**:657, 1890.

time the number has increased each year, there being twenty cases, with three deaths, in 1927.

PREEPIDEMIC CASES

The preepidemic cases were apparently of two main types, the one developing as a complication of the acute specific fevers, the other being of the poliomyelitic type of infection and involving the brain. Although the former type is usually described as a complication of the acute specific fevers, cases occur secondary to any respiratory infection. The onset is acute and usually occurs with high fever, coma and convulsions. The convulsions may be generalized but are usually unilateral. The course of the disease is stormy and terminates in a few days or slowly improves. Those recovering often have sequelae in the nature of hemiplegia and altered intelligence varying from slight changes to low grade idiocy. Examinations of the brains reveal hemorrhages of varying degrees and extent. Although there is no definite pathologic entity as such, these cases are designated as acute hemorrhagic encephalitis.

The following case illustrates this type of disorder.

CASE 1.—T. C., a white boy, aged 3½ years, was well except for a slight cold of a few days' duration prior to admission to the Children's Memorial Hospital on June 13, 1925. There was a sudden onset of projectile vomiting. A few hours later the right side of the face began to twitch, followed a few hours later by twitchings of the right arm and leg. On admission the patient had a temperature of 104.6 F., and was comatose; horizontal nystagmus, the quick component to the right, an injected swollen nasal pharynx, a few coarse râles in the lungs and a slight rigidity of the neck were present. The following day the left side of the body as well as the right was spastic, and many small petechial hemorrhages were found on the body. The spinal fluid was clear under increased pressure and contained 30 cells per cubic millimeter; the Pandy test was positive; the fluid showed 152 mg. of sugar; the Wassermann reaction was negative. On the second day the twitchings on the right side ceased, as did the nystagmus, but the right pupil was much larger than the left. At times there was a Babinski sign on the left. After a few days the sensorium gradually returned to normal, and the other neurologic symptoms disappeared except for a marked right-sided hemiplegia which has persisted to date. The boy is backward mentally and presents a behavior problem. Although it was impossible to determine definitely, he was probably of normal intelligence before the illness.

As already stated, polio-encephalitis or, more exactly, poliomyelo-encephalitis was the other common type of the disease encountered before the epidemic. Although it is generally a comparatively rare disease, many cases occurred during the late summer and fall of 1927. The onset is usually subacute, with headache or vomiting or both. The cerebral symptoms depend on the area of the brain chiefly involved—medulla, pons or cortex. If the cortex is chiefly involved, there is a markedly changed sensorium; if the medulla is chiefly involved, there may be none. The changes in the cranial nerves also depend on the

localization of the infection. Evidence of meningeal irritation accompanied by weakness of the muscles of the neck is an important symptom in differentiating poliomyelo-encephalitis from other forms of encephalitis. Evidence of a peripheral flaccid paralysis may be slight. A predominance of polymorphonuclear cells in the spinal fluid is often present at the beginning of the disease.

The following case illustrates this type of encephalitis:

CASE 2.—S. B., a white boy, aged 11 years, was admitted to the Children's Memorial Hospital on Aug. 14, 1927, with a history of having been well until two days before admission. At that time he developed abdominal distress with projectile vomiting and headache. These symptoms were followed twenty-four hours later by gradually developing difficulty in swallowing and diplopia. Twenty-four hours later, he was unable to talk or swallow anything. On the day of admission to the hospital, he also developed a rather marked facial paresis and complained of pains in the extremities. He had a slight fever but did not appear especially ill. On examination there was a marked paresis of the right sixth and seventh cranial nerves, a slight horizontal nystagmus and at times a complete inability to talk or swallow. The soft palate and uvula were not entirely paralyzed; there was a rather marked rigidity of the neck and marked head drop, and breathing was entirely abdominal. The knee jerks were not obtained during the first two days at the hospital but later returned; the pulse rate was 96. Examination of the spinal fluid showed: cell count, 5; sugar, 72 mg.; globulin tests, negative, and the Wassermann and colloidal gold tests, negative. This boy presented the picture, then, of a mild polio-encephalitis with marked involvement of the midbrain. Improvement was slow. Seven months after the illness, the facial paresis was still present; his speech was somewhat indistinct, and he had a slight difficulty in swallowing.

EPIDEMIC ENCEPHALITIS

The epidemic of encephalitis introduced new clinical and pathologic syndromes as well as characteristic sequelae. Although the condition had been described many times, a brief summary is included for purposes of comparison. The onset is subacute or slow and is secondary to or associated with influenza or respiratory infections. Lethargy, ocular paralyses, involvement of the seventh nerve in a large number of cases, changes in the deep reflexes and fever usually are present. The patient often has a masklike expression. The lethargy is often followed by a prolonged insomnia. These cases run a fairly constant course. The neurologic symptoms are constant, and the general picture does not usually change during the course of the illness. The brains are edematous and congested and have minute hemorrhages in the gray matter about the base of the brain, the third ventricle, the aqueduct of Sylvius, the optic thalamus, the pons and the medulla. Intense perivascular infiltration with lymphocytes, plasma cells and a few polymorphonuclear cells; proliferation and degeneration of nerve cells are present. The changes in the cortex are slight. There is little meningeal change.

An undeterminable number of those recovering from the acute illness develop sequelae; nearly 50 per cent of those developing sequelae do not give a history of encephalitis. For reasons unknown, a correlation does not exist between the severity of the acute illness and the time of onset, or the character or severity of the sequelae. The sequelae fall under two general groups: the parkinsonian-like syndromes and behavior disturbances. Metabolic disturbances with increase in weight, associated with neurologic symptoms characteristic of lethargic encephalitis, have recently been reported by Walsh [5] and others. Although Grossman reported their occurrence in 17 per cent of a series of eighty-nine cases, I have seen only one definite case in about 275 cases of encephalitis of all types in children. The neurologic manifestations of the sequelae vary from slight changes, such as unequal sluggish pupils and possibly paresis of the seventh nerve, to extreme changes seen in paralysis agitans with tremor, masklike expression, stiffness of gait, slowness of movement, slow, scanning speech and muscle rigidity accompanied by marked ocular changes. There is apparently no correlation between the severity of physical changes and the severity of the obesity or behavior disturbances, that is, cases showing the most extreme neurologic symptoms may not show any behavior disturbances, and I had two cases of extreme behavior disturbances that did not show any neurologic symptoms for many months.[6] The behavior changes are entirely emotional and are so characteristic that they can often be recognized at first glance. These children have a characteristic anxious, overalert, strained expression. Periods of extreme excitability, accompanied by deep pauseless breathing and uncontrollable temper tantrums, often occur. It is important to note that there is no disturbance of intelligence, for many years, at least.[7]

As previously stated, most of the children with encephalitis coming under observation during the past four or five years do not belong in any of the foregoing groups. A large percentage have clinical and pathologic characteristics as well as sequelae unlike any of the foregoing types and sufficiently uniform to indicate an entirely different form of the disease. In 1925, Brown and Symmers [8] reported ten cases of a rapidly fatal disease in children attended by symptoms referable to the

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5. Walsh, Thomas G.: Postencephalitic Obesity, J. A. M. A. **87**:305 (July 31) 1926.

6. Beverly, B. I., and Sherman, Mandel: Postencephalitic Behavior Disturbances without Physical Signs, Am. J. Dis. Child. **27**:565 (June) 1924.

7. Sherman, Mandel, and Beverly, Bert I.: The Factor of Deterioration in Children Showing Behavior Difficulties After Epidemic Encephalitis, Arch. Neurol. & Psychiat. **10**:329 (Sept. 23) 1923.

8. Brown, C. L., and Symmers, D.: Acute Serous Encephalitis, a Newly Recognized Disease of Children, Am. J. Dis. of Child. **29**:174 (Feb.) 1925.

central nervous system, under the title of "Acute Serous Encephalitis." The authors stated: "The naked eye and histologic changes in the brain of all the patients were monotonously alike." In all cases they found an intense edema and congestion of the brain. Microscopically, they found hyperemia and edema of the pia-arachnoid, engorgement of the blood vessels, perivascular and pericellular edema with or without vacuolation of the ground substance and acute cloudy swelling of the pyramidal cells. In places they found numerous glia cells lying in what appeared to be a vacuole but which represents an area of edema. Kemkes and Saenger [9] reported seventy-two cases of encephalitis in children, studied between June, 1920, and February, 1926. Of these, twelve were definitely diagnosed as epidemic encephalitis, seventeen as doubtful cases, ten as cases of encephalitis following acute infectious diseases, and thirty-three as cases of encephalitis of undetermined etiology. Recently, Grinker and Stone [10] reported pathologic studies of a group of children having a fatal disease with symptoms referable to the central nervous system and found changes which they thought were characteristic of toxic encephalitis. The reports of Brown and Symmers and of Stone and Grinker pointed out a pathologic entity characterizing toxic encephalitis. Both reports dealt with fatal cases only. During the past four years I have made careful clinical studies in about forty cases which I feel should be classified as toxic encephalitis. Twelve of the patients died, and the brains of five were studied histologically by Dr. George B. Hassin. Dr. Hassin also made valuable suggestions for clinical study which have been included in this paper.

From the group of cases studied, I feel that toxic encephalitis presents a clinical as well as a pathologic picture, which makes it recognizable and distinguishable from the other types of encephalitis in most instances. This type is characterized by an acute onset, secondary to an infection of the respiratory tract, a changed sensorium ranging from a mild stupor to a prolonged coma and frequently changing neurologic symptoms of varying severity and duration, often the patient has a toxic appearance and in some cases there is a general picture of profound toxemia. Convulsions, high fever and evidence of meningeal irritation may be present. As in all forms of encephalitis, increased sugar and globulin are almost invariably present in the spinal fluid. The number of cells in the fluid may be normal or increased to several hundred per cubic millimeter. The clinical course is usually stormy and may terminate fatally or with complete recovery in a few hours or it may go

9. Kemkes, B., and Saenger, S.: Encephalitis in Children, Monatschr. f. Kinderh. **32**:334 (June) 1926.

10. Grinker, Roy R., and Stone, T. T.: Acute Encephalitis in Children, Arch. Neurol. & Psychiat. **20**:244 (Aug.) 1928.

on for days. An accurate prognosis is extremely difficult, except that it is generally known that most patients recover. Recovery may be complete or attended with sequelae.

The pathologic condition of toxic encephalitis is different from that of lethargic encephalitis and offers an explanation for the clinical symptoms. The changes in the brain in epidemic encephalitis are essentially inflammatory and are restricted largely to the basal ganglia. Those of toxic encephalitis are toxic or chemical and noninflammatory. All parts of the brain are affected, especially the cortex. Marked edema is apparently present in all cases, and Dr. Hassin has suggested that this may be the cause of death in many cases. Instead of the perivascular infiltration of lymphocytes about the blood vessels found in the epidemic type there are liquefaction of the parenchyma of the brain and degenerative changes in the ganglion and glia cells, the extent depending on the duration and severity of the disease.

Kemkes and Saenger reported thirty-three cases of encephalitis out of a series of seventy-two in which the etiology was undetermined. All of my cases showed evidence of an infection of the respiratory tract which was thought to be the avenue of infection. There seems to be little correlation between the severity of the respiratory infection and the extent of involvement of the brain. The most severe forms of encephalitis sometimes occurred as complications of mild colds, while the mildest forms sometimes occurred as complications of severe respiratory infections with pneumonia or severe gastro-enteritis.

Epidemic encephalitis and poliomyelo-encephalitis are characterized by involvement of the cranial nerves which is persistent and late in disappearing. This is what one would expect, since the pathologic changes are largely in the midbrain and are of inflammatory nature. In toxic encephalitis, on the other hand, the changes in the midbrain are slight and are in the nature of toxic or chemical irritations of the brain and may be transient. This apparently accounts for the marked variability and changeability of the condition of the cranial nerves present in a large percentage of cases of severe toxic encephalitis. A divergent strabismus may change to a convergent strabismus within a few hours or from day to day. In some cases the inequality of the pupils changes several times during the examination. The most severe cases may be attended with little, if any, change in the cranial nerves, except perhaps a mild optic neuritis. As previously stated, the changes in the cranial nerves frequently completely disappear long before the changed sensorium.

The foregoing points are illustrated by the following cases:

Case 3.—Andrew B., a white boy, aged 3 months, was admitted to the Children's Memorial Hospital in October, 1924. He was well until two days previous to admission, when he developed severe vomiting and an infectious diarrhea. On admission to the hospital he appeared toxic and acutely ill. He was restless and

irritable. The respirations were deep and pauseless. Tissue turgor was fair. The white blood count was 41,000. The fontanel was not bulging. Because of a slight rigidity of the neck and a semicomatose condition, a spinal puncture was done. The spinal fluid was clear, with a cell count of 6, a slight trace of globulin and 105 mg. of sugar. On the second day in the hospital, the vomiting ceased and the diarrhea was much improved. The right ear drum was bulging, and pus was obtained on paracentesis. The pupils became somewhat unequal, and a marked bilateral strabismus developed. Both of these symptoms changed often. On the fifth day in the hospital the gastro-enteritis was much improved; the symptoms of acidosis disappeared, but the patient developed frequent generalized clonic convulsions. Marked rotary nystagmus, internal strabismus and inequality of the pupils were present. All of these conditions changed many times during the examinations. The right pupil, for instance, would be much larger than the left for a few minutes, and vice versa. The temperature was normal on admission to the hospital but after the first two days ranged from 103 to 105 F. Two days later the convulsions stopped, but the symptoms in the eyes were still present. On the eighth day in the hospital, bronchial pneumonia developed. There was a marked rigidity of the whole body, and breathing was of the Cheyne-Stokes type. Except for the inequality of the pupils, the condition of the eyes disappeared. The fontanel was slightly bulging for the first time. A spinal puncture done a few hours before death revealed a cell count of 35 and 93 mg. of sugar.

Autopsy, reported by Dr. William G. Hibbs, showed: disseminated bronchial pneumonia, generalized anemia, cloudy swelling of the myocardium and of the kidneys, marked fatty changes of the liver, hyperemia and edema of the brain, edema of the leptomeninges, unequal pupils, bilateral mucopurulent otitis media, Meckel's diverticulum, marked postmortem rigidity and lividity, slightly depressed fontanel and negative cultures of the spinal fluid.

Dr. George B. Hassin reported the following microscopically: The cerebellar pia was markedly infiltrated with lymphocytes; the parenchyma of the brain was liquefied; the blood vessels, especially in the motor area, were proliferated; the ganglion cells showed neuronophagic phenomena; the glia in some cases showed broken up nuclei and appeared ameboid-like; there were fatlike substances in the ganglion cells and in the blood vessels. The microscopic diagnosis was marked toxic encephalitis.

Case 4.—Irwin D., a white boy, aged 3 years, was admitted to the Children's Memorial Hospital on Aug. 13, 1925, with the history of having been well until the day before admission, when he developed diarrhea and a slight fever. On the morning of admission he became comatose, had generalized clonic convulsions, a temperature of 105 and many watery stools. On admission to the hospital, he had pharyngitis and infectious diarrhea. He was comatose and spastic. Horizontal and vertical nystagmus and a positive Babinski sign were present. He died a few hours after admission. Dr. William G. Hibbs reported the following conditions found post mortem: A pseudomembranous ileocolitis, edema of the brain and cloudy swelling of the kidneys. Dr. Hassin, who examined both brains at the same time, reported that the changes were the same as those in case 3.

The marked changes which may go on in the brain with only slight clinical manifestations are illustrated by case 5.

Case 5.—Charles W., a white boy, aged 3½ months, was admitted to the Children's Memorial Hospital on May 27, 1926, with a history of having been well until about a week previous to admission. During the week he cried a great deal

but was described as otherwise normal. On the day before admission he had a generalized clonic convulsion lasting about fifteen minutes and many watery stools. Except for the diarrhea, moderate dehydration, a red swollen pharynx and general toxic appearance, the physical examination was entirely negative on admission to the hospital. During the first day in the hospital, the infant had several generalized clonic convulsions. A spinal puncture revealed a normal cell count and no globulin. The white blood cell count was 25,000; the blood platelet count was 110,000, and the bleeding time was fourteen minutes. Fifty cubic centimeters of whole blood was given intramuscularly. Three days later, the convulsions having stopped and the general condition having improved in the meantime, he became stuporous. The fontanel became bulging and tense, the knee jerks brisk, and the neck slightly rigid. A spinal puncture done the following day showed a cell count of 190 and positive globulin. The culture and Wassermann test on the spinal fluid gave negative results; the spinal fluid showed 52 mg. of sugar. On the seventh day in the hospital, the blood platelet count was 240,000 and the bleeding time four minutes. There were occasional gross twitchings of the extremities; the diarrhea and general condition, including stupor, were much improved. On the twentieth day in the hospital, the spinal fluid showed 6 cells and no globulin. The patient was doing well and was considered sufficiently recovered to be discharged from the hospital. He did well at home, and as far as could be determined from the history given by cooperative and intelligent parents was entirely well for eight days. On the ninth day vomiting and diarrhea began; he was brought to the hospital in deep coma, having clonic convulsions, and died a few hours later. The temperature during the whole course of the illness was between 99 and 102. On postmortem examination, Dr. Hibbs found: A marked edema of the leptomeninges, hyperemia and edema of the brain, cloudy swelling of the myocardium, liver and kidneys, moderate fatty changes of the liver, slight hypostatic hyperemia and edema of the lungs, hyperemia of the mesenteric lymph nodes and fibropurulent otitis media on the right side. Cross-sections of the brain revealed areas of softening, ranging in size from that of a pinpoint to 1.5 cm., throughout both hemispheres. Microscopic sections examined by Dr. Hassin revealed numerous areas of softening which were likely of degenerative nonvascular origin.

That all cases of toxic encephalitis do not come to a fatal termination is illustrated by case 6.

Case 6.—F. M., a boy, aged 8½ years, was admitted to the Children's Memorial Hospital on Dec. 27, 1926, with a history of having had a severe cold for a few days and becoming acutely ill with fever and generalized clonic convulsions the day before entrance to the hospital. On admission he was in deep coma, had a temperature of 104 F. and a condition in the chest suggestive of bronchial pneumonia. There was a moderate rigidity of the neck, exaggerated deep reflexes, a suggestive Babinski sign at times and transient inequality of the pupils. The spinal fluid contained 30 cells; the test for globulin was positive and the culture and Wassermann reaction were negative. The condition of the chest and the neurologic symptoms, except the coma, disappeared in a few days. For nearly two weeks, however, the boy was stuporous and most of the time could not be aroused. After two weeks the sensorium gradually cleared, and he was discharged apparently well a week later. He was followed for about six months. During that time neurologic symptoms did not occur, nor as far as could be determined did changes in personality or intelligence take place.

Case 7.—C. R., a white boy, aged 5 years, was seen in consultation with Dr. B. C. Walton on Oct. 11, 1927. He was well until a few days previously, when

he was one of several members of the family to develop a moderately severe cold. Three days later he developed a high fever and became comatose. When examined on the following day he was in deep coma and could not be aroused. The knee jerks were exaggerated but equal; pathologic reflexes were not listed. Changes in the cranial nerves were not present, except a possible slight injection of the vessels of the optic disks. Demonstrable rigidity of the neck or head drop were not present. The pharynx was intensely red and swollen. The spinal fluid was clear and under slightly increased pressure. After five or six days the coma gradually disappeared; the boy began talking rationally, and the temperature was normal. He was very weak. It was several weeks before he could walk again and when last seen, five months after the illness, was still having some difficulty in walking, due to a disturbance in equilibrium. Otherwise he was apparently entirely well and as far as could be determined had not suffered any change of intelligence. Except for the slight difficulty in walking, the neurologic examination gave entirely negative results.

The discussion thus far has been concerned with severe cases of toxic encephalitis presenting a clinical picture which can be explained only on the basis of marked cerebral involvement. There remains a much larger group of cases showing less severe and more transient neurologic symptoms. A frequent neurologic examination of sick children often reveals a condition indicative of slight involvement of the central nervous system. In many of these cases a diagnosis of toxic encephalitis seems justifiable; in the state of present knowledge, other borderline cases leave a diagnosis in doubt. As most of these patients recover, the aid of the neuropathologist is denied. The following cases illustrate the problem:

Case 8.—C. W., a white girl, aged 4 years, was brought to the Children's Memorial Hospital with a history of having been well with the exception of a slight cold of a few days' duration. About an hour before admission, she was semicomatose and irritable when aroused. On admission she became unconscious; breathing was loud, deep and rapid. At times there was a marked bilateral internal strabismus, inequality of the pupils, exaggerated deep reflexes and a bilateral Babinski sign. These symptoms changed many times during the examination. Within three hours after admission, all signs of neurologic involvement, including the changed sensorium, had disappeared and the child remained well. The spinal fluid was normal. It seems unlikely that a true inflammation sufficient to cause these symptoms could clear up in such a short time; transient toxic encephalitis, secondary to the infection in the throat, is more probable.

Case 9.—L. R., a white boy, aged 18 months, was seen on Jan. 10, 1928, because of an acute respiratory infection. He had a temperature of 103.5 F., a red, swollen pharynx and a few coarse râles in the lungs. Two days later it was noted that he preferred to lie with his head buried in the pillow, seemed to have a headache and was irritable. He had a rather stupid, dull expression, which was different from his previous and subsequent appearance. The knee jerks were brisk but equal. Pathologic reflexes were not elicited. The condition of the eyes was significant. He had little control over the muscles of the eyes. A divergent strabismus and at times a convergent strabismus were present, and at times one eye turned in, and the other turned up and out. Twenty-four hours later coordination of the muscles of the eyes was practically normal, and two days later

all of the neurologic symptoms had disappeared. A spinal puncture was not done. The neurologic condition developed after the acute stage of the respiratory infection had passed, the temperature being below 102 F. and the chest being almost entirely normal. Since the illness he has been entirely well. It seems probable that in this case, as in case 8, the symptoms were produced by a transient noninflammatory irritation of the brain.

The question next arises as to whether children developing convulsions at the onset of an acute infection with high fever and without subsequent neurologic symptoms should be classed as having toxic encephalitis. I do not believe that any one has demonstrated changes in the brain in these cases. It is known that a child can have large numbers of convulsions without evidence of the changes in the brain found in encephalitis. This is well illustrated in uremia and meningitis. It seems probable that toxic encephalitis has a specific cause—possibly due to specific toxins.

A sufficient number of patients with toxic encephalitis who have recovered from the acute illness have not been followed and carefully studied to determine the frequency and nature of the sequellae. Many instances of mentally defective children in whom the intelligence changes apparently followed the acute illness, which was probably encephalitis have been encountered. The following case of idiocy was unquestionably due to encephalitis.

CASE 10.—S. L., a white girl, aged 3 years and 2 months, was of normal intelligence previous to her admission to the Children's Memorial Hospital in October, 1924. She entered the hospital with a history of having been well until a few days previously, when she developed a fever and had a few convulsions. On admission she was comatose, had a temperature of 103.5 F., and appeared acutely ill. Except for evidence of nasopharyngitis, the general physical examination gave negative results. Mild, transient neurologic symptoms were present in addition to the coma. A spinal puncture revealed a cell count of 6 and a slightly positive Pandy reaction. At the end of five days she was removed from the hospital against advice, but her case was followed up at home. After a few weeks, the coma had entirely disappeared, but she had poor memory and acted like an infant. She was not able to sit up for nearly six months; she could not walk for ten months, and at the age of 5 years could say only a few words. About six months after the illness convulsions developed, and when she was last examined, about six months before this paper was written, she showed evidence of further deterioration. Definite conclusions cannot be based on a single case, and the possibility of this case being one of hemorrhagic encephalitis must also be considered.

SUMMARY

1. The increase in the incidence of encephalitis in children is apparently due to new or previously unrecognized clinical and pathologic syndromes.

2. Previous to 1918, there were two main types of the disease: acute hemorrhagic encephalitis and poliomyelo-encephalitis.

3. The epidemic of encephalitis introduced new clinical and pathologic syndromes with characteristic sequelae.

4. The increasing frequency of encephalitis since the epidemic is due largely to toxic encephalitis, which has clinical and pathologic characteristics differing from the other types.

5. The symptoms of toxic encephalitis are largely referable to changes in the cortex.

6. The pathologic changes in toxic encephalitis are largely in the cortex and indicate toxic or chemical—noninflammatory—changes.

7. Most patients with toxic encephalitis recover. The sequelae are now being studied.

30 North Michigan Avenue.

Pediatric Biographies

PHILIP GERHARD GRÜLING
1593-1667

JOHN RUHRÄH, M.D.
BALTIMORE

Any one who practiced medicine in Germany in the seventeenth century, and who desired a "practical" book on the diseases of children might and probably would have bought Grüling's little book on the subject. It is not an important contribution, but it is interesting as an example of the books which were in use at that period.

Grüling was born in 1593, at Stolberg on the Harz. He studied medicine, and for a short time settled in Nordhausen, where he rendered noteworthy service in the plague epidemic of 1626. The following year he went back to his native town, and spent the remainder of his life there. He was an important personage in Stolberg, where he was physician to the Count Stolberg and at one time Burgomeister.

Grüling was a rather prolific writer, and among his contributions was a work on chemistry and the various preparations used in medicine. It is entitled "Floriiegiam Hippocratico-chymicum novum," Leipzig, 1631. It was popular and was reprinted in 1644 and 1665. He also wrote "Von der Pest," which was published in 1659 by a printing establishment in Nordhausen. Other publications are: "De calculo et suppressione urinae," Nordhausen, 1662 and 1668; "Medicinae practicae libri quinque, etc.," Nordhausen, 1668; "Observationum et curationum medicinalium dogmatico-hermaticarum," 1668; "De triplici in medicina universalis, evacuationes genere et in specie," 1671; "Tractatus novus, von Weiberkrankheiten," in deutsches Artznei-Buch, 1676. In 1680, some years after his death, a collected edition of his works was issued in Leipzig.

His little book on children is in German and is entitled, "Philippi Grülingii, Gräffl. Hoff- und Stadt-medici in Stolberg am Hartze, Tractat von Kinderkranckheiten und allerhand beschwerlichen zufällen woher sie kommen, was daraus zu urtheilen und wie solche curiret werden können: Alles durch selbst eigene Erfahrung observirt, und jedermänniglich zu Nutz in Druck gegeben, Anno M.D.LX., zu Nordhausen bey Johann-Erasmus Hynisch zu finden."

The book, as he stated, is the result of his own experience, and in the preface he observed that he might have made it longer but feared that

PHILIPPI GRÜLINGII

Gräffl. Hoff- und Stadt-Medici in Stolberg am Hartze/

TRACTAT

Von

Kinder Kranckheiten/ und allerhand beschwerlichen Zufällen/

woher sie kommen/ was daraus zu urtheilen/ und wie solche curiret werden können:

Alles durch selbst eigene Erfahrung observirt, und jedermänniglich zu Nutz in Druck gegeben

ANNO M. DC. LX.

Zu Nordthausen/
bey Johann-Erasmus Hynitzsch zu finden.

if he did it would be unpleasant for the readers. Would that some of our present-day writers might emulate him in this!

He also stated that he undertook to write the book because physicians were seldom called in to see children, and in consequence, many were injured by following the advise of beggars, midwives and other forward women.

The book is divided into forty short chapters, of which the first three deal with the care of the infant and the others with various diseases, symptom-complexes or symptoms. For example, there are chapters on constipation, belly-ache, on weakness in children, vomiting in young children, wakefulness, night terrors, measles and chickenpox (which he calls *"Bocken"*), diarrhea, stopping of the nose, worms, umbilical hernia, coughing and sneezing, fever and great heat in children; there is one chapter on "when a child is ill and one does not know what from."

The book is highly pragmatic. The author devotes practically no space to theoretic considerations; only a word or two states some cause generally accepted at the time. The book consists largely of recipes and therapeutic advice, the former lengthy, the latter brief.

CHAPTER XXVII

VON DER SCHWINDSUCHT ODER DORRE DER JUNGEN KINDER (ON PHTHISIS OR CONSUMPTION OF YOUNG CHILDREN)

Cause of the Same

Consumption often comes from a hot fever, from worms, from running off of the body (diarrhea) and other things which withdraw the nourishment from the limbs.

The Cure of the Infirmity

Distill the water from the lung of a red or black calf and administer a spoonful often and rub the joints with it warmed.

If you want to do more add the blood of the calf to chicken or other things edible.

Little tragacanth cakes are very good in this. Give the child seven mornings, one after the other, each morning 3 betony grains in mush or otherwise.

There is nothing better than bathing the child in goat's or cow's milk or cook three sheep's heads in fresh beer until they are ready to fall apart and bathe (the child) in the soup. There is a little herb which grows on the oak called *Haedera*, of this a water may be distilled and the child given every day 3 spoonsful of this or powder it and give in pap or violet juice, one sample every morning, or the chest may be smeared with chicken fat.

A water may also be distilled from *filice* or ferns and made into a syrup with sugar *Candi* and given frequently. It can not harm if one fills little pillows with it and lets (the child) sleep on them.

News and Comment

UNIVERSITY NEWS

Tulane Establishes a Behavior Clinic.—The school of social work of Tulane University, New Orleans, has established a behavior clinic for children. It is not expected that purely medical cases will be dealt with at this clinic, but that the dean will appoint physicians to take charge of the medical treatment of the patients.

Assistance to English Speaking Physicians.—The American Medical Association of Vienna will greatly assist any English speaking physicians who wish to take courses at the university. The address is: American Medical Association of Vienna, Vienna VIII. Alserstrasse 9, Austria.

Appointments and Promotions.—The regents of the University of Oregon have made the following appointments in the faculty of the medical school: Dr. James W. Rosenfeld, associate clinical professor of pediatrics, and Dr. Lendon H. Smith, associate clinical professor of pediatrics.

Dr. G. Carriere, previously chief of the pediatric clinic, has taken the chair of clinical medicine; his place in pediatrics has been taken by Dr. J. Minet, formerly professor of therapeutics.

Promotion to the grade of Officer of Legion of Honor has been accorded to Dr. Julien Huber, physician of Salpêtrière, and treasurer of the pediatric society to Dr. G. Carriere of the faculty of Lille University and to Dr. E. Terrien, previously chief of Children's Clinic in Paris.

The University of Chicago clinics opened in October, 1927, are soon to be enlarged by the addition of the new Bobs Roberts Memorial Hospital for Children, and a new hospital for crippled children.

Western Reserve University School of Medicine announces the reappointment of Dr. Henry J. Gerstenberger as head of the department of pediatrics and contagious diseases.

Appointments in the Faculty of Medicine at Marseilles include: chief of the children's clinic, Dr. G. Perrimond; assistant, Dr. Poinso, chief of the infants' clinic, Dr. George Sesqués; assistant Mlle. Julie Cousin.

The following appointments have been made in Paris: Dr. M. P. Fèvre is named chief of Professor Ombrédanne's clinic. At Professor Lereboullet's clinic at the Hospice des Enfants Assistes, Dr. Lelong and Dr. Brizard are named chiefs of the clinic. In Professor Nobecourt's service at the Hôpital des Enfants-Malades, Dr. René Martin is named assistant chief of the clinic. Dr. B. Weill-Halle is named to replace Dr. Lereboullet at the Hôpital des Enfants-Malades. Dr. G. C. Paisseau is named to take Dr. B. Weill-Halle's place at the Hôpital Herrold.

RUSSIAN PEDIATRICIANS CELEBRATE ANNIVERSARIES

Dr. N. Lounine celebrated his anniversary of fifty years of practice at St. Petersburg recently. Dr. Lounine is 77 years old. He was a pupil of Rauchfuss, and followed him in the direction of the childrens' hospital "Karl Rauchfuss."

Dr. J. Winocouroff is celebrating his fortieth anniversary as director of the children's clinic at the Medical Institute of the city of Odessa.

RESIGNATION OF DR. BONNESS

Dr. Hazel D. Bonness, director of the child welfare division of the state board of health of Montana for several years, has resigned because of ill health.

DEATHS

Professor Hirota, died in Tokyo on Nov. 27, 1928, at the age of 70. He was the first to occupy the chair of pediatrics in the Medical Department of Tokyo Imperial University, and was a pioneer in this specialty in many extramural activities. In 1892 he organized a society for the study of diseases of children, and in 1895 he founded a pediatric publication under the name of *"Sho-ni-kwa"* (Pediatrics). His efforts along this line formed the basis of a later development which culminated in the organization of the Japanese Pediatric Society, having as its organ the *Journal of Pediatrics,* a monthly journal publishing the researches in pediatrics. Professor Hirota was also a pioneer in socializing the services of trained pediatricians among the poor and needy, as in 1891 he was instrumental in the organization of the Women's Mutual Child Health Association. In order to perpetuate the varied contributions of Professor Hirota, his pupils and friends have placed his bronze statue in the university. In 1916 he retired from active duty and was made professor emeritus; his active interest continued to be manifest, however, as he was the head of the Japanese Pediatric Society, a position he had held for thirty-three years. His contributions to research comprise many papers on infantile beriberi and encephalitis.

Leopold Baumel, formerly professor of the Children's Clinic in the Faculty of Montpelier, died recently at the age of 75.

D. N. Paton, professor of physiology of the University of Glasgow, and co-worker with Prof. Leonard Findley of that city, died at the age of 69.

Antonio Abate, in the department of pediatrics at the University of Catania, died recently.

Carlos Lagos Garcia, recipient of the prize of the Institute Mitre, Buenos Aires, Argentina, died recently, just before receiving the prize.

Christos Malandrinos, professor of pediatrics at the University of Athens, is dead at the age of 65. He was a corresponding member of the Society of Pediatrics of Paris, and founder of the chair of clinical pediatrics at the University of Athens, which he occupied until his death.

Prof. Clemens Pirquet, head of the Department of Pediatrics at the University of Vienna, was reported to have died suddenly in his native city on March 1, 1929. Professor Pirquet for two years was head of the pediatric department at Johns Hopkins University. He afterward returned to Vienna, where he took the chair on Echericsh's death. He was widely known for his skin test in tuberculosis, but among pediatricians, the work leading up to the test and the later work on nutrition are regarded as outstanding.

Correspondence

To the Editor.—With reference to my article on "Vincent's Infection of the Nose" which appeared in the AMERICAN JOURNAL OF DISEASES OF CHILDREN, August, 1928, vol. 36, pp. 352-356, I wish to state that Hubert M. Jay reported a case of Vincent's infection of the sinus in a man, aged 29, with a positive nasal smear. This case report appeared in the *"Medical Journal of Australia,"* Oct. 8, 1927, vol. 2, pp. 513-514.

HAROLD I. SHULMAN, M.D., Boston.

Abstracts from Current Literature

Anatomy and Physiology

THE SELLA TURCICA. ARTHUR SCHULLER, Am. J. Roentgenol. **16**:336 (Oct.) 1926.

The size and shape of the sella turcica are not criteria as to the condition of the pituitary gland. Destruction of the sella is found in such inflammatory processes of the sphenoid body as osteomyelitis, syphilis or tuberculosis, and in malignant conditions of the region and intracranial processes, usually tumors starting in the brain, the pituitary gland, the cranial nerves or the arteries. Differentiation between invasion of the sphenoid body by a malignant or an inflammatory process and erosion of the sella due to pressure is easier than differentiation between the erosion of the pituitary fossa caused by general intracranial pressure and the enlargement of the sella due to localized tumors. The points of differentiation are: 1. In cases of general pressure, the floor of the sella is usually single; when localized tumors are present two or three outlines of the floor are often seen, because these localized processes often lie asymmetrically. 2. The anterior clinoid process in cases of general pressure is usually thin; in the presence of localized tumors it is normal or thicker. 3. In localized tumors, calcification is often seen in the region of the sella.

STULIK, Chicago.

VARIATIONS IN THE SIZE OF THE RED BLOOD CORPUSCLES IN NEW-BORN AND IN YOUNG INFANTS. HEISZEN and SCHALLOER, Ztschr. f. Kinderh. **46**:105 (July) 1928.

In the physiologic anisocytosis of new-born and young infants, the large cell elements, the macrocytes, predominate. The average range of diameter in the child during the first few days and weeks after birth is from 8.5 to 9.3 microns, contrasted with that of 7.5 microns in adults. In the infant, the difference between the greatest and smallest diameters ranges from 6 to 8.2 microns; in adults, 2.5 microns. Morphologically, the red and white cell picture of newly born infants agrees wholly with the regenerative picture of simple posthemorrhagic anemia in healthy adults. The erythrocytes of the newly born infants, in contrast to those of adults after the loss of blood, are distinguished by a normal content of hemoglobin. They are to be regarded, therefore, as cells which are equal in function to the ripe erythrocytes. The anisocytosis of newly born infants is not a phase of an active erythropoiesis set in action by birth and new conditions of life. It is also a characteristic of fetal blood. For this reason it must be regarded as an extension of the fetal condition to the period immediately after birth and as an expression of the common immaturity which is also characteristic of the tissue cells.

EMERSON, Boston.

Pathology, Bacteriology and Biochemistry

STUDIES ON THE EFFECT OF ROENTGEN RAYS ON GLANDULAR ACTIVITY: V. THE EFFECT OF ROENTGEN RAYS ON EXTERNAL PANCREATIC SECRETION. B. H. ORNDORF, J. I. FARRELL and A. C. IVY, Am. J. Roentgenol. **16**:349 (Oct.) 1926.

Experimenting with dogs, the authors found that in one animal one tenth of the human erythema dose increased the concentration of lipase and trypsin, but did not affect the quantity of secretion. In two animals, one-half the human erythema dose increased the quantity and the total output of ferments; while in a third animal, the quantity of the secretion and of the ferments increased during the first week after exposure, following which the quantity of secretion and the total amount of lipase decreased and the total amount of trypsin remained normal. The human erythema dose decreased both the quantity of secretion and the total

ferments for two weeks in two animals. Although the function is temporarily injured by the erythema dose, a return to normal gradually results. In these experiments, the tail of the pancreas was transplanted under the mammary gland so that other organs were not greatly interfered with during irradiation.

STULIK, Chicago.

THE INTESTINAL BACTERIA AND THEIR CLINICAL SIGNIFICANCE IN THE INFANT. EUGENE STRANSKY, Rev. franç. de pédiat. **4**:143, 1928.

After an extensive review of the literature on the intestinal flora, Stransky presents his own experience in this field. He supports the views of those who maintain that the secretion of the upper part of the small intestine is normally "bacteriostatic." This is in accordance with his idea of the interdependence of the general resistance and the number of organisms present in the small intestine. The presence of organisms in the small intestine is not a cause nor yet a result of an intestinal disturbance, but is the result of a general disturbance which has changed the normal secretion. In conclusion, the author devotes several pages to a description of the bacterial content of the large intestine, and effect of various foods on the types of flora.

LESLIE, Evanston, Ill.

THE NORMAL AND PATHOLOGIC METABOLISM OF THE NUCLEOPROTEINS AT VARIOUS AGES. D. PACCHIONI, Riv. di clin. pediat. **26**:249, 1928.

A general discussion of the subject is presented. The literature on the subject is reviewed and a bibliography included.

VARIATIONS IN THE AMOUNTS OF POTASSIUM AND CALCIUM IN THE SERUM AND IN NEUROMUSCULAR EXCITABILITY FOLLOWING THE INJECTION OF EPINEPHRINE HYDROCHLORIDE, ATROPINE AND PILOCARPINE. V. ZAMORANI, Riv. di clin. pediat. **26**:288, 1928.

From seven to nine experiments on rabbits were made with each drug. Epinephrine hydrochloride was found to cause a decrease in the potassium and calcium content of the blood serum. The electrical excitability of the neuromuscular system was increased in certain animals and diminished in others.

Atropine caused a diminution in the amount of the potassium but not in the calcium of the serum. The electrical excitability was increased.

Pilocarpine caused a diminution of potassium and an increase in the calcium of the serum. The electrical excitability was usually increased.

PHARMACODYNAMIC RESEARCH IN CHILDREN. G. HALFER, Riv. di clin. pediat. **26**:569, 1928.

The author attempted to test the relative reactions of the sympathetic and parasympathetic systems in children. Epinephrine was used as a sympathetic drug, and ergotamine and pituitary as parasympathetic drugs. Observations were made of blood pressure, pulse rate, respiration, patellar reflex, temperature and differential white blood count before, and fifteen and thirty minutes after, the injection of the drugs. Forty children were used in these observations.

Healthy children react to those substances which excite the sympathetic and to those which excite the parasympathetic system. In the majority of cases, the response of the sympathetic system is more intense in children more than 3 years of age, and that of the parasympathetic system more intense in children less than 3 years of age.

VARIATIONS OF TOTAL NITROGEN, OF UREA-NITROGEN AND OF AMINO-NITROGEN IN THE BLOOD OF INFANTS. NOEMI CIAMPI, Riv. di clin. pediat. **26**:666, 1928.

Observations were made on twenty-three infants, seven of whom were breast fed, two partially breast fed and fourteen artificially fed. The following table summarizes the results.

Results of Study on Total Nitrogen, Urea-Nitrogen and Amino-Nitrogen in the Blood of Infants

	Total Nonprotein Nitrogen, Mg. per 100 Cc.	Urea-Nitrogen, Mg. per 100 Cc.	Amino-Nitrogen, Mg. per 100 Cc.*
Breast feeding	320–329	164–250	58–99
Mixed feeding	313–422	200–303	65–197
Artificial feeding	390–635	302–427	67–188

* Includes amino acids, ammonia and other nitrogenous products insoluble in ether-alcohol and not precipitated by phosphomolybdic acid.

The results obtained from blood taken during the second hour of digestion show more nitrogen than that taken during the first and third hours.

HIGGINS, Boston.

DESTRUCTION OF THE EPIPHYSIS AND PREMATURE CALCIFICATION OF THE AREA OF GROWTH IN LONG BONES. C. T. WILLICH, Beitr. z. klin. Chir. **142**:626, 1928.

The increase in length of long bones depends on the growth of the epiphysis, an enchondral ossification. An interstitial growth of long bones does not contribute in any way to the increase in length of long bones. Any process influencing the epiphysis will interfere, therefore, with the process of ossification. Not only trauma but both acute and chronic infections and nutritional disturbances exert a decided influence on the growing epiphysis. Among the nutritional disturbances, rickets more than any other disease produces disturbances of growth in the long bones. It is most prevalent during early childhood and puberty, the time of most active growth, and any damage which it causes persists even after the rachitic condition heals.

The extent to which rachitic disturbances are responsible for the disturbance in enchondral ossification and length of bone growth has not been definitely established. That additional causes exist cannot be doubted. Von Neurath and von W. Müller reported a case in which a child with one leg paralyzed from anterior poliomyelitis developed rickets. Subsequently, the lame leg grew longer than the normal leg, perhaps because of less weight, use and muscle pull. This same inequality of growth in the length of long bones may be caused experimentally by producing a defect in the long bone and changing the muscle pull and weight bearing angle.

Certain deformities occur in rickets that cannot be explained on a mechanical basis. Certain forms of coxa valga in the late stage of rickets, for example, frequently disclose evidence of endocrine disturbances. Periosteal and endosteal ossification in rickets are not hampered as is the enchondral ossification. Even in the earliest stages, there are frequent evidences of excessive periosteal ossification.

Chondrodystrophy fetalis is responsible, far more than rickets, for stunted growth in the length of long bones. Since this condition occurs rarely as compared with rickets, the author employed rachitic subjects in his clinical and pathologic studies. Twelve children were studied who were disproportioned dwarfs. The deformities did not come into evidence until the second or third year. The children did not begin to walk until the third or fourth year. The etiology of epiphyseal destruction and premature calcification of the area of growth is difficult to determine. Whether it is embryologic from mechanical means or on an endocrine basis is still undetermined. The endocrine factor certainly bears a definite relationship to the dwarfed condition.

The roentgen examination of the femur in this series of patients showed ossification of the epiphyseal growing end. The epiphysis turned acutely posteriorly. In some instances a bowing gave the vara phase and, occasionally, even a torsion. A few cases disclosed such conditions as exostoses of the metaphyses. There were other conditions of the tibia usually seen in rickets, such as a saber sheath deformity.

When one compares these observations with those in chondrodystrophy, in the latter, the bony epiphyses may have disappeared completely or they may be small, atrophic, irregular masses. Luxations and subluxations occur because of the looseness of the epiphysis or the destruction of the epiphysis in the joint. The deformities resulting from this condition, therefore, are much more marked than those produced by rickets.

Because of the lack of conclusive evidence in establishing the etiology of epiphyseal destruction and premature calcification of the growing area, the author sought experimental proof. He was able to produce a deformity in dogs and rabbits much like, if not identical with, rickets in the human being, by displacing the epiphysis posteriorly to the popliteal space, which insured the greatest amount of mechanical pressure on the growing zone. He was thus able to obtain a dwarfed femur which yielded practically the same gross and microscopic anatomicopathologic data found in the rachitic human being. The author attributes the deformities obtained in animals largely to trauma — not that resulting from the operation in displacing the epiphysis posteriorly, but the later trauma from the sinking in of the upper fragment into the lower. This process occasions the gradual destruction of the growing zone and leads to early ossification and cessation of growth in the length of the long bones. It was found that when the epiphysis was shifted forward or to either side, producing a valgum or varum, fewer disturbances of growth occurred. In this investigation an explanation was not found for the etiology of chondrodystrophy fetalis.

From a study of the literature, of his own clinical material and of the data secured by investigation, the author made the following deductions: 1. Even though there may be a superficial similarity between the deformities caused by rickets and by chondrodystrophy there is, nevertheless, a distinct difference. 2. During the course of rickets of the lower end of the femur, either bilateral or unilateral, with displacement of the epiphysis posteriorly, a premature ossification of the growth area results with a cessation of growth in length and the development of a disproportioned dwarf. 3. In experiments on animals, by excision of a wedge-shaped piece of bone from the posterior third of the epiphyseal line at the growing zone and then displacement of the epiphysis backward a premature ossification and cessation of growth resulted. This was noticed both clinically and experimentally and showed a relationship between the deformity and cessation of growth and the displacement posteriorly of the epiphysis and sinking of the upper into the lower fragments. 4. It was established microscopically in experiments that only when there was not a complete separation of the epiphysis and diaphysis but only a sliding and notching, with a displacement of the epiphysis toward the popliteal space, a period of widening of the epiphyseal line and growing zone occurred, soon followed by a rapid ossification of the growing zone.

OBERHELMAN, Chicago.

ACTION OF THYROXIN ON THE GLYCOGEN CONTENT OF THE LIVER AND SKELETAL MUSCLE OF GUINEA-PIGS. O. BÖSL, Biochem. Ztschr. **202**:299 (Nov.) 1928.

The author made injections into guinea-pigs of 0.2 mg. of thyroxin daily for five or six days. Animals which kept quiet lost weight even though they ate enough food. There was no change in the amount of muscle glycogen, but a marked decrease occurred in the glycogen content of the liver. If the diet was increased and the dosage of thyroxin decreased, there was less, if any, loss of glycogen in the liver. If the amount of food was only half that required by a normal animal, the glycogen content of the skeletal muscle was diminished and the liver did not contain any glycogen. When the animals were active and their intake of food was not limited, the glycogen content of both the liver and the muscle was increased.

BRAHDY, New York.

THE FUNCTION OF THE PARATHYROID. K. WALTNER, Monatschr. f. Kinderh. **40**:317, 1928.

From experiments based on recent literature, the author advances the following interesting theory concerning the parathyroids: The parathyroid secretion is similar in many respects to insulin. Lack of insulin results in great increase in blood sugar, in the emptying of the deposits of glycogen and in glycosuria. Excessive parathyroid secretion increases the amount of blood calcium, empties the deposits of calcium and causes the increased excretion of calcium. With an excess of insulin, the amount of blood sugar diminishes, the glycosuria stops, but the deposits of glycogen continue to become depleted. Insufficient parathyroid secretion diminishes the amount of blood calcium; although the calcium balance is positive, the osseous system loses calcium, probably to the muscles. In other words, insulin and parathyroid secretion mirror each other. Since surplus as well as insufficient dosage of parathyroid causes a loss of calcium in the bones, it is obvious that this hormone must be used with care.

BLOOD CATALASE IN SICK AND WELL CHILDREN. M. FUKUYAMA, Monatschr. f. Kinderh. **40**:441, 1928.

The blood catalase varies so greatly in health and likewise in disease without any seeming relationship to the nature and severity of the ailment that as yet it is of little clinical value.

THE RUSSNYAK METHOD OF EXAMINING PLASMA PROTEIN. J. C. SCHIPPERS, Monatschr. f. Kinderh. **40**:521, 1928.

Using the micromethod described by Russnyak, the author studies the globulin and fibrinogen fractions in the blood of a number of sick children. Although the method itself is open to objections, he believes it fairly accurate. His results are so variable, however, that he does not find the method of any clinical use. He offers the interesting suggestion that perhaps the albumins and globulins of the blood are not absolutely as constant in their structure as supposed.

GERSTLEY, Chicago.

EXPERIMENTAL FORMATION OF RENAL CALCULUS THROUGH THE ABSENCE OF VITAMIN A. S. PERLMANN and WEBER, München. med. Wchnschr. **75**: 2167, 1928.

The authors have previously reported finding renal calculi in rats fed on diets lacking in vitamin A. In the series reported at this time, they used 100 rats: 33 received a diet lacking in vitamin A; 15 received a diet without vitamin A, but to which milk was added; 15 received a diet without vitamin A, to which cod liver oil was added, and 37 received a normal diet. Five of the first group died in less than sixty days. The formation of the first calculus was observed after eighty days. After five months, when all the rats were killed, seven showed calculi; all these, however, belonged to the first group. Thus, calculi were not found in animals fed on a diet lacking vitamin A, if milk or cod liver oil was added or when a normal diet was given.

The authors do not claim that the absence of vitamin A alone is the cause of the formation of renal stone, for infection and reduced vitality may be factors.

SCHORER, Kansas City, Mo.

THE BLOOD PHOSPHATE CURVE OF THE NORMAL AND THE RACHITIC ORGANISM. J. WARKANY, Ztschr. f. Kinderh. **46**:1 (July) 1928.

On the exhibition of inorganic phosphate, the normal organism reacts with an increase in the inorganic serum phosphate. By the use of 0.5 Gm. of secondary sodium phosphate per kilogram of body weight, the increase amounts on the average to 3.4 mg. per hundred cubic centimeters. With the same dose, the

rachitic child shows an extremely small increase, on the average, only 0.4 mg. per hundred cubic centimeters. In other words, the blood phosphate curve of rachitic children is considerably flatter than that of the normal subject. This condition can be changed for a few days by the use of irradiated ergosterol.

THE INFLUENCE OF INFUSIONS OF ISOTONIC SOLUTIONS ON RESPIRATION. H. BAER, Ztschr. f. Kinderh. **46**:45 (July) 1928.

Baer studied the question of whether or not the basal metabolism was altered by the subcutaneous and intraperitoneal injection of different isotonic saline solutions (0.9 per cent salt solution, physiologic solution of sodium chloride and Ringer's solution) and found that with a sufficient intake of water a rise in the metabolic rate does not occur either in the infant or in the rabbit or dog, nor is the basal metabolism influenced. The fever, which occurs after the injection of isotonic salt solution made as usual with distilled water, is not a real salt fever or, perhaps, better not a salt hyperthermia. It must be looked on rather as a fever from the infection produced by bacteria and bacterial toxins (the so-called water deficit) which possesses even in the prodromal stage the characteristics of an increased formation of heat.

EMERSON, Boston.

VISCOSITY OF THE BLOOD IN INFANTS. W. MIKULOWSKI and H. CHMIELEWSKA, Acta paediat. **8**:185 (Aug. 15) 1928.

Using the Hess viscosimeter, the authors made 144 determinations on blood from 100 patients ranging in age from 1 to 15 years. At the same time, they observed the blood pressure, hemoglobin, counts of red and white cells, refractive index and total protein content. In normal persons the blood viscosity, on comparison with water, gave a reading of from 4.5 to 5 when a disease was present, on the other hand, the viscosity varied between 2 (for certain anemic states) and 12 (in one case of myelogenous leukemia and one of morbus ceruleus). An elevated viscosity in the presence of normal or low blood pressure was found often in circulatory disturbances such as leukemia, cardiac insufficiency with valvular disease, chronic pulmonary conditions, during convalescence from severe forms of acute infections and in circulatory asthenia.

MCINTOSH, Baltimore.

Nutrition

BUTTERMILK VERSUS LACTIC ACID MILK IN ATHREPSIA. A. B. MARFAN and M. CHEVALLEY, Nourrisson **16**:257 (Sept.) 1928.

Lactic acid milk alone or as a complement to breast milk was fed to eleven poorly nourished infants ranging in age from 11 days to 1 month. In five cases the lactic acid milk was poorly tolerated, producing vomiting, diarrhea and a dermatitis of the buttocks. In the other six cases difficulty was experienced in getting the infants to take sufficient quantities, and the increments in weight were small. The authors obtained superior results with buttermilk, especially when it was partly neutralized with lime water.

MCCLELLAND, Cleveland.

IMPORTANCE OF THE QUANTITATIVE RELATIONS OF THE COMPONENTS OF FOOD; RESEARCH ON A FEEDING MIXTURE FOR INFANTS. G. GUASSARDO, Riv. di clin. pediat. **26**:649, 1928.

In the pediatric clinic of the University of Genoa, several feeding mixtures are used. The author has made analyses of the chemical composition of two of these mixtures and compared the results with those of mother's milk and cow's milk. The mixture M. A. B., which the author believes is the better, has the following constituents: butter, 10 Gm.; olive oil, 15 Gm.; malt preparation, 30 Gm.; sugar, 15 Gm.; lactose, 10 Gm.; casein, 5 Gm.; milk, 350 cc., and water, enough to make 1,000 cc.

Comparative Analysis of the Mixture M. A. B. and Human Milk and Cow's Milk

	M. A. B., Per Cent	Human Milk, Per Cent	Cow's Milk, Per Cent
Protein	1.35	1.36	3.24
Fat	3.97	3.90	3.81
Carbohydrate	7.03	6.77	4.62
Dry residue	13.16	12.31	12.50
Calcium oxide	0.073	0.038	0.172
Calcined magnesia	0.009	0.007	0.021
Potassium oxide	0.083	0.063	0.184
Sodium oxide	0.031	0.018	0.069
Phosphorus pentoxide	0.100	0.036	0.221
Chlorine	0.028	0.036	0.101
Ash	0.340	0.203	0.744

The figures for human milk and for cow's milk are collected from various sources. HIGGINS, Boston.

MILK SUGAR IN THE METABOLISM OF THE GROWING ORGANISM. M. STEUBER and A. SEIFERT, Arch. f. Kinderh. **85**:12 (Aug. 31) 1928.

By calculating the amount of nitrogenous material, pure fat and mineral in the milk given in the test cases and checking against the same material eliminated in the feces and urine, the authors were unable to prove that any synthetic fat was formed in the organism from milk sugar. Furthermore, milk sugar is not capable of replacing biologic fat in the metabolism of the child.

MINERAL METABOLISM IN CHILDREN. E. ROMINGER, Arch. f. Kinderh. **85**:23 (Aug. 31) 1928.

This is the third article of the series and deals with the mineral balance of the dystrophic infant. The author found that mineral metabolism is greatly affected by the daily excretions. Frequent stools would therefore cause considerable change. This is especially true of the calcium retention in dystrophy. It may not be low enough to cause any considerable clinical manifestations of rickets or spasmophilia, but a change in the daily excretion of stools would lower it below the threshold value. An excess of calcium in the diet of the dystrophic infant has the same favorable quality of retention that it has in the normal child.

THE ACTION OF ULTRAVIOLET LIGHT ON THE NOURISHMENT AND GROWTH OF THE CHILD. H. KOEPPE, Arch. f. Kinderh. **85**:81 (Sept. 28) 1928.

This is the eighth article of this series and deals with the action of ultraviolet light in hastening oxidation. In testing the action of ultraviolet light on cod liver oil, it was found that the resulting oxidation was spontaneous but accelerated. The hemolysis occurring after the action of ultraviolet light is an accelerated spontaneous hemolysis following the action of oxidation.

THE ACTION OF ULTRAVIOLET LIGHT IN THE NOURISHMENT AND GROWTH OF THE CHILD. S. RAGIB, Arch. f. Kinderh. **85**:97 (Sept. 28) 1928.

This is the ninth article of this series and deals with the action of ultraviolet light on oils. The point of attack and the mechanism of the activity of ultraviolet rays on cod liver oil, sesame oil and olein are studied. Apparently the action is in the nature of an oxidation of the unsaturated acids and, in addition, a photohydrolytic saponification. The formation of acid caused by the rays was found to be approximately proportional to the duration of the irradiation and to the size of the irradiated surface. Neither the height of the column of cod liver oil nor the temperature had an influence on the action of ultraviolet rays.

SANFORD, Chicago.

PHYSIOLOGIC CRANIOTABES. M. LUBECK KLOTZ, Monatschr. f. Kinderh. **40**:518, 1928.

The author does not agree with Rosenstern and Bruns that craniotabes is always a sign of rickets. He believes that there are some breast fed children who show softness of the bones of the cranium between the first and third months but who do not show any signs of rickets clinically, roentgenologically or in blood chemistry and who do not develop rickets later.

THE TREATMENT OF RICKETS WITH IRRADIATED ERGOSTEROL. S. A. GIL, Monatschr. f. Kinderh. **40**:527, 1928.

There is no question that irradiated ergosterol has a powerful influence in curing those who have rickets. Some authors have reported that it may be dangerous at times. Gil believes that much more work must be done to establish a definite dosage. He also advances the theory that the drug may benefit the bones by calling calcium and other minerals from the tissues. The bones absorb the calcium but leave an excess of potassium in the blood. Such an excess may cause irritability of the nervous system. Under these circumstances it would be wiser to give calcium compound by mouth in addition to the irradiated ergosterol. Gil tested this theory on five rachitic children.

Chemical studies of the blood showed that the amount of blood calcium increased more rapidly in those patients receiving irradiated ergosterol with calcium. As these patients seemed to thrive better both clinically and roentgenologically than the others, Gil believes that irradiated ergosterol should always be combined with some calcium and phosphorus.

GERSTLEY, Chicago.

THE CALORIC VALUE OF FOODS FOR INFANTS. K. HILLE, Ztschr. f. Kinderh. **46**:36 (July) 1928.

Tables giving the caloric value of foods for infants, though indispensable, would be more valuable and less conducive to error if there were less variation in the foods most often used. For example, the value given to human milk varies from 56.5 to 87.7 calories per hundred cubic centimeters in different tables — in the case of cow's milk, from 50 to 74 calories. A variation also can be found in a table dealing with dilutions of cow's milk plus carbohydrate, and in such foods as butter meal and Eiweissmilch. The tables given by Hille are acknowledged not to be perfect and are the result of an attempt to set up a standard. Researches should be made to establish the average caloric value of cow's milk. Investigators should be explicit as to the content of the mixtures which they give and should exclude personal and local customs of feeding.

EMERSON, Boston.

THE EFFECT OF CASEIN CURD AND OF EGG ON THE ACID-BASE BALANCE OF INFANTS. V. RANTASALO, Acta paediat. **8**:1 (Aug. 15) 1928.

On the basis of studies of the stools and urine, the author endeavored to determine the acid-producing effect of certain foods. His patients were normal infants from 2 to 9 months of age. Preceding the test periods, he made determinations of the p_H of the stools and measured the volume for twenty-four hours, the specific gravity, p_H, total nitrogen, ammonia nitrogen, total acids, organic acids and total phosphorus of the urine. In the test periods, which usually lasted five days, an isocaloric portion of purified casein, or of egg, was substituted in some cases for part of the butter or carbohydrate of the diet during the foreperiod; in other cases, the food to be tested was added to the diet of the foreperiod without substitution. Daily determinations of the before-mentioned factors were then carried out. The results are reported in great detail not only with regard to individual analyses but also after the calculation of the various coefficients of excretion. The author finds that casein raises the p_H of the stools, while egg lowers it. Both casein and egg increase the total ammonia nitrogen of the urine, the titratable acids, organic acids and p_H; on the other hand, casein lowers the ammonia, total acid and organic acid coefficients, while egg raises them.

MCINTOSH, Baltimore.

Prenatal Conditions

CASE OF CONGENITAL DISLOCATION OF THE PATELLA. W. ROWLEY BRISTOW, Proc. Roy. Soc. Med. **21**:77 (July) 1928.

The author presented a girl, aged 6 years, with congenital dislocation of the patella, in order to ask the members what treatment they would advise and at what age it should be undertaken.

ACHONDROPLASIA OF THE THIRD GENERATION. DONALD HUNTER, Proc. Roy. Soc. Med. **21**:1321 (June) 1928.

The author describes fully a case of achondroplasia in a girl, aged 7 years. He also describes her father, who had achondroplasia, and his father who, according to descriptions, also had achondroplasia.

DWARFISM. A. G. MAITLAND-JONES, Proc. Roy. Soc. Med. **21**:1326 (June) 1928.

The author reports the case of a girl, aged 3 years and 10 months, who was born at full-term and weighed 1 pound and 10 ounces (737.1 Gm.) at birth. Teeth erupted at 6 months; she sat alone at 6 months, talked at 16 months and walked at 2 years and 4 months. There was no history of dwarfism in the family. When the paper was written, the child weighed 9 pounds and 12 ounces (4,422.5 Gm.). Her height was 26 inches (65.9 cm.). The head was 15 inches (37.5 cm.) in circumference. Although the child was so small, it had the appearance of age.

THE CLINICAL ASPECT OF CONGENITAL MESENTERIC MALFORMATION IN CHILDREN. GEORGE E. WAUGH, Proc. Roy. Soc. Med. **21**:1717 (Aug.) 1928.

Congenital malformations of the mesentery are a definite morbid entity of a chronic type which may be recognized, before operation, by careful clinical investigation. The symptom complexes to which they give rise cannot be explained by reference to any of the well known abdominal surgical diseases, still less by any purely functional disability which may be included under the term "indigestion." The most important physical sign is the emptiness of the right iliac fossa, associated, sometimes, with an asymmetrical enlargement of the abdomen on the left side. These signs follow of necessity, as the whole segment of the embryonic midintestine is involved in a failure of rotation and fixation after reduction from the umbilical sac. Roentgen investigation should prove to be more helpful in confirming the clinical diagnosis when the special method of examination described is used as a routine. Operative treatment may cure the patient; alternatively, it may reveal a pathologic condition for which a rational course of treatment may be drawn up subsequently, when the precise details of the malformation have been discovered.

WILLIAMSON, New Orleans.

A CASE OF MICROMELIA. MARTINHO DA ROCHA, JR., Arch. Pediat. **1**:33 (Nov.) 1928.

A case of chondrodystrophy fetalis is described, and roentgenograms and photographs are presented. The possibility of various etiologic factors, such as endocrine deficiency, thymus, maternal hyperthyroidism and syphilis, is discussed.

A CASE OF ACONDROPLASIA. W. TORELLÓ-CENDRA, Soc. Catalana de Pediat., Nov. 24, 1927, reprinted, Barcelona, 1928.

The author presents a case of acondroplasia, with photographs and roentgenograms. He believes that a series of cases in which numerous roentgenograms have been made may give some idea of the etiology. A good bibliography of both the French and the Spanish literature is given.

SANFORD, Chicago.

AGENESIS OF ABDOMINAL MUSCLES. TAIELLEUS, Nourrisson **16**:291 (Sept.) 1928.

Agenesis of the abdominal muscles is a rare congenital anomaly; reports of only twelve such cases were found in the literature, and the author adds one more. Only males are affected. The intestinal loops are visible through the thin abdominal wall, and in one instance dilated ureters could be seen. The liver, spleen, kidneys and the entire bladder could easily be palpated. The defect is always bilateral. Postmortem examination showed the presence of rudimentary muscle fibers, indicating a muscular hypoplasia rather than complete absence. Associated defects are cryptorchidism, dilatation and hypertrophy of the bladder and ureters, enteroptosis and anomalies of the umbilicus.

McCLELLAND, Cleveland.

CONGENITAL ATRESIA OF THE INTESTINE. RICHARD SCHMIDT, Arch. f. klin. Chir. **149**:510, 1928.

From a review of the literature, the author arrives at the following classification of intestinal atresias in respect to location: (1) at the distal ileum in the region of the ductus omphalomesentericus; (2) at the ileocecal valve; (3) in the duodenum in the region of the ampulla of Vater and, (4) on rare occasions, at the junction of the jejunum and ileum. The author reports three cases from the children's surgical clinic at Leipzig. One child had multiple atresias of the small bowel with a mesenteric defect; another had a simple atresia or stenosis for a considerable distance of the small bowel, and a third, atresia of the large bowel.

After a microscopic study of this material, the conclusion was reached that the etiologic factor in congenital atresias is an interference with the circulation of the bowel. Experimental work seems to indicate this fact. One cannot wholly deny, however, the existence and influence of the fetal intra-abdominal pressure which results in an encroachment on the room for growth allowed the abdominal organs.

ANAL ATRESIAS WITH AN EXTERNAL FISTULA IN COMBINATION WITH PREPUTIAL ANOMALY AND CONGENITAL DISLOCATION OF THE HIP JOINT. RICHARD SCHMIDT, Arch. f. klin. Chir. **149**:523, 1928.

According to the author, the frequency of congenital anal anomalies is about 1 in 10,000; 24 per cent of these are associated with vestibular fistulas, and 5 per cent with perineal, scrotal and suburethral fistulas. The anomalies occur more often in girls than in boys.

A boy, aged 3 days, whose parental history was unimportant, had an anal atresia with a perineal fistula which was operated on. The microscopic observations were different from those of other investigators in that the entire tract was lined with stratified squamous epithelium and the tract opened into the rectum.

The same child had a bilateral congenital dislocation of the hip and a preputial anomaly. In attempting an explanation for such a series of anomalies in one person, the author states that the determination of the various anlages occurs at different periods of development. This may originate in the ovum. Location and size of the anlage are determined by the influence of the growth of one part on another. A disturbance of one part definitely interferes with the normal sequence of events; as a consequence, other associated anomalies occur.

THE FORMATION OF CONGENITAL ATRESIA AND STENOSIS OF THE SMALL INTESTINE. O. HAHN, Beitr. z. klin. Chir. **142**:252, 1928.

The writer reviews the various theories of the causation of congenital atresias and stenosis of the small intestine described in the literature of the last fifty or more years. These theories are divided into three classes: developmental, inflammatory and mechanical. Even these factors may be secondary to some unknown factor which remains obscure.

From a careful review of about 250 cases in the literature, however, the author arrives at the following conclusion: 1. The formation and development of congenital duodenal atresia are clearly established, according to (*a*) the theory of Tandler and Krenter and modified by Forssner, which consists of the statement that a physiologic duodenal atresia occurs between thirty and sixty days of intrauterine life; (*b*) the theory of Beneke-Karpa, in which the process of differentiation in the development of the liver is assured to proceed too far; (*c*) the theory of Beneke-Fanconi, in which the process of differentiation is said to be incomplete, and (*d*) the theory of Anders who thinks that a generalized disturbance of the correlation of growth is a basis for the disturbed development of the duodenum.

2. The formation of congenital atresia of the small bowel (exclusive of the duodenum) is still obscure. All evidence, however, seems to point to a disturbance of the reposition of the physiologic hernia of the umbilical cord. This reposition occurs normally by the rotation of the umbilical cord which is a physiologic process. By this rotation the content of the hernia of the umbilical cord is mechanically replaced in the abdominal cavity. A disturbance, therefore, in the sequence of this rotation of the umbilical cord results in an abnormal reposition of the loops of bowel in the physiologic hernia. This process, if excessive, produces a complete artesia or, if mild, produces only minor intestinal damage.

OBERHELMAN, Chicago.

THE DEVELOPMENT OF PREMATURE CHILDREN. JULIUS FRANKE and ERICH SINGER, Monatschr. f. Kinderh. **40**:496, 1928.

This is a statistical review of premature infants examined at the age of 3 or more years. The writers considered the weight, height, nutritional index (Pirquet), condition of the blood, dentition, rachitic signs, mentality, infections, etc. They found that in general premature infants do well. They emphasized that the important factor in insuring good results is to give the child proper nutrition and to prevent infections during the early months. Proper nutrition is accomplished by the use of breast milk supplemented with some whey to increase its mineral content.

GERSTLEY, Chicago.

THE FACTORS OF INHERITANCE AND ENVIRONMENT IN STUDIES OF TWINS. J. LANGE, Ztschr. f. Kinderh. **34**:377, 1928.

This article should be read by everyone who is studying twins. Lange discusses the well known similarity of mono-ovular twins, pointing out that they are rarely identical but may often display striking differences. These dissimilarities, however, are rarely fundamental and may easily be explained by parakinetic factors. The value of the article lies in the fact that it dispenses with complicated mechanisms of asymmetrical inheritance in the attempt to account for the dissimilarity of mono-ovular twins. Lange discusses the following influences which he believes may simulate the effect of dissimilar germ plasms: unequal nutrition of fetuses in utero, intoxications of the fetus due to disease of the mother, influence of labor on the first twin born, disease of the individuals affecting through chance different parts of the body or organ, e. g., hemorrhages in the central nervous system due to pertussis, chance variations in the severity of infectious diseases or variations in the time of their occurrence — an infection occurring at puberty may delay the onset of sexual maturity and so influence the personality of the individual permanently. Much superficial dissimilarity may be caused by the attempt of the twins, often stimulated by relatives, to differ from one another. Lange offers striking instances of twins with exactly the same character anlage whose actual life histories differed greatly because of the influence of their strong willed wives.

REICHLE, Cleveland.

Diseases of the New-Born

RESUSCITATION FROM ASPHYXIA IN THE NEW-BORN AND OTHERS: ITS CONTROL AND TREATMENT. YANDELL HENDERSON, New England J. Med. **199**:977 (Nov. 15) 1928.

In cases of electric shock, drowning and similar forms of acute asphyxia, the author considers it of primary importance to institute artificial respiration immediately. Artificial respiration by Schafer's manual prone pressure method is declared preferable to the use of any type of pulmotor. The delay involved in sending for apparatus is generally fatal. Furthermore, the prone pressure method probably provides a more effective means of moving air in and out of the lungs than does apparatus which produces a positive pressure and which is liable to inflate the stomach and injure the lungs.

Besides the consideration of forms of acute asphyxia, there is the much larger problem of gradual asphyxia. Practically all deaths are finally due to asphyxia; respiration fails, the supply of oxygen to the blood, and thus to the tissues, ceases, and life comes to an end. The final failure of respiration in infectious and chronic diseases may be delayed; but as yet no physiologic therapy, other than oxygen inhalation in pneumonia, is available which is of much more than temporary effectiveness. Fortunately, between acute asphyxia and gradual asphyxia, to which no treatment as yet known is applicable, there are a number of conditions which are simply and effectively treated by the application of the modern physiologic knowledge of respiration.

The treatment is inhalation of oxygen containing carbon dioxide to stimulate breathing. It has been used to resuscitate new-born infants who fail to breathe or in whom respiration gradually diminishes and comes to a standstill a short time after birth. These failures of breathing are deserving of study. They frequently appear to be due to intracranial hemorrhage. In a study of these cases, it is significant that in adults who have undergone operations on the brain the inhalation of carbon dioxide may prevent failure of breathing. In other cases failures of breathing are due to the drugs which the mother has received to ease her pains. Morphine, scopolamine, chloroform, ether and other drugs of this nature pass to the child through the placental circulation. They tend to prevent or diminish spontaneous breathing in the infant. In physiologic terms, they depress the sensitivity of the respiratory center to the stimulus normally afforded by the blood gases. A higher pressure of carbon dioxide is therefore required to induce breathing.

The author refers to the work of his colleague, Dr. B. C. Sword, anesthetist in Grace Hospital, New Haven. Dr. Sword has an attachment on his anesthesia apparatus which is so arranged that after delivery, while the mother is anesthetized for repairs, the respiration of the child may be stimulated by an inhalation of oxygen and carbon dioxide. It is noteworthy that in some cases, 5, 10 or 15 per cent or even higher concentrations of carbon dioxide are beneficial and, indeed, even necessary.

The author also suggests that medical societies arrange to have the city fire or police department and the hospital ambulances equipped with the H-H inhalator. The apparatus may then be sent for whenever any form of asphyxia occurs in either adults or infants.

GENGENBACH, Denver.

DYSENTERIFORM DIARRHEA: TREATMENT OF NEW-BORN INFANTS WITH ACETARSONE, AND ENEMAS OF A FLAIRINE DYE. P. CHEDID, Bull. Soc. de pédiat. de Paris **9**:473 (Nov.) 1928.

Good results are reported in seven cases of diarrhea with bloody stools, supposed not to be due to amebas or to *Bacillus dysenteriae*. A brand of acetarsone by mouth in doses of 1 cg. three or four times a day; enemas of 0.1 Gm. of a flairine dye in 500 cc. of water were also used in most cases. About forty-three other cases are mentioned, but controls or failures are not reported.

CLAUSEN, Rochester.

THE IMPORTANCE OF PHYSIOLOGIC CHOLEMIA IN THE PRODUCTION OF ICTERUS NEONATORUM. P. LEREBOULLET, Paris méd. **2**:384 (Nov. 3) 1928.

The author considers that at present the physiologic bilirubinemia of new-born infants is a demonstrated fact; when this bilirubinemia becomes pronounced, it produces icterus and the bilirubin content may reach figures that are much higher than those found in adults. In a series of hematologic studies begun twenty-seven years ago, a constantly large amount of bile was found in the blood of new-born infants. Lereboullet observed that in specimens of blood from infants with icterus neonatorum the proportion of bilirubin differs, varying from 1:500 to 1:2,100; in three cases it was greater than 1:900, the ratio which expresses the maximum amount of bilirubin found in blood from icteric adults. Even in new-born infants without icterus, an appreciable cholemia was found during the first few days after birth. This is to be explained by the following facts: 1. The mass of blood of the new-born infant is relatively small. 2. The volume of the liver in the new-born infant is relatively much larger than that in the adult, and the organ can therefore elaborate relatively more bilirubin. The author also found that in the blood of the umbilical cord there is a relatively high percentage of bilirubin which, however, is less than that in the fetus or the new-born infant. The blood of the mother frequently contains more bilirubin than does normal blood (about 1:30,000 instead of 1:36,500). Mother's blood, therefore, contains only one-third as much bilirubin as the blood of the umbilical cord. These facts prove that the blood in the umbilical arteries gives up a part of its bilirubin to the maternal blood; the umbilical cord, therefore, represents the excretory route of the pigments which cannot be eliminated by the kidney or the intestine, and its ligation results in the physiologic hypercholemia of new-born infants.

SANFORD, Chicago.

ARE VARIATIONS IN BIRTH WEIGHT DEMONSTRABLE STATISTICALLY FOR DIFFERENT SEASONS? K. HELLMUTH, Ztschr. f. Geburtsh. u. Gynäk. **93**:147, 1928.

This article contains some important ideas concerning statistical variations, namely, the arithmetical mean and the dispersion and average error of the arithmetical mean. These mathematical ideas, it is shown, may be used to determine statistical variations and may be applied to the solution of certain medicobiologic problems.

The author analyzed 13,853 births from the standpoint of statistical variation. The births were taken from the records of three different years and divided according to the month in which each occurred. The average number of births for each month was 385.

The author did not find any evidence to confirm the conclusion of Abels that the birth weight varies with the month of the year in which the birth occurs. He did not consider seasonal variations in birth weight statistically demonstrable. The results did not appear to show any difference in the birth weight or body development of infants delivered at full term which could be due to variations in the maternal diet during the winter and summer months. The author stated that if Abels would make an analysis of his own material according to proper statistical methods, he would probably reach the same conclusion.

He considered that the attempt of Abels to influence the size of the fetus by the diet of the mother was not justified by the opinion that the difference in the maternal diet during the winter and summer months was responsible for the supposed seasonal variations in birth weight and development of newly born infants delivered at term.

OSTEOGENESIS IMPERFECTA. E. KLAFTEN, Ztschr. f. Geburtsh. u. Gynäk. **93**:167, 1928.

Osteogenesis imperfecta is rarely observed, especially in viable infants. These infants show the same tendency to spontaneous fractures that is seen in adults with osteopsathyrosis idiopathica. Opinions differ as to whether or not these

two conditions are the same; von Recklinghausen makes a sharp distinction between them, but recent observations of Sumita and others indicate that the two conditions are identical. In chondrodystrophia foetalis there is a defective development of bone from cartilage, whereas in osteogenesis imperfecta there is defective bone development from the periosteum and endosteum which causes the fragility of the bones. Meyer believes that milder forms of this disease are seen in such conditions as defective development of the skull bones.

The author reports in detail a case of a hydrocephalic infant weighing 1,400 Gm., delivered at term. The placenta showed cysts and an old infarct which made up about one fourth of its area. The mother gave a history and physical evidence of rachitis. The roentgenograms showed defective bone development and a lessened deposit of calcium.

The author considers that the presence of rachitis in the mother and the placental changes are of importance in this case. He inclines to the belief that this condition results from some disturbance of fetal metabolism.

He cites two cases: one observed by Zurhelle, in which osteogenesis imperfecta was present in both mother and offspring; and another described by Kusnetzhof, in which one twin had this condition and the other was normal. In the case which he observed, he suspects a familial tendency to defective bone formation and, due to the placental degeneration, deficient nutrition and a disturbed metabolism of the bone forming cells.

ADAIR, Minneapolis.

NUCLEAR ICTERUS (KERNIKTERUS) OF THE NEW-BORN INFANT. G. HUWER, Ztschr. f. Geburtsh. u. Gynäk. **94**:150 (Sept.) 1928.

Huwer's report deals with twins delivered spontaneously at term and apparently normal at birth. There was no history of jaundice or other abnormalities in the other children or the parents. Three hours post partum the infants were distinctly icteric, but were otherwise well for forty-two hours. Then both infants suddenly collapsed, became cyanotic, made shallow, infrequent attempts at respiration and died an hour later. There were no convulsions. Observations at autopsy were similar in the two cases. The gallbladder and its ducts were normal. The liver did not show any abnormality except a high content of hemosiderin. The spleen was large and dark red. The parenchyma of the lung was normal but contained a yellow secretion. The rest of the thoracic and abdominal viscera as well as the meninges were normal. The nucleus lentiformis and the nucleus caudatus were yellow, in contrast with the surrounding tissue. The nuclei in the hippocampus major, tegmental region, cerebellum, medulla, olives and cord at all levels were distinctly yellow. Microscopic examination showed that the yellow color was due to stained glial structure around the injured ganglion cells.

Beneke is the only authority who thinks that the condition is due to an infection. The author feels that it is a congenital or hereditary abnormality of the hematopoietic system resulting in intravascular destruction of the blood which begins during the intra-uterine period.

BRAHDY, New York.

Acute Infections

THE HEART IN INFECTION. HOMER F. SWIFT, Am. Heart J. **3**:629 (Aug.) 1928.

Diseases of the heart are divided into (1) the infectious, roughly found in the first four decades of life, and (2) the degenerative, which appear later. In diphtheria there is a toxic damage to the muscle fibers, and involvement of the conduction system is frequent. In scarlet fever, there may be (1) toxic involvement of the heart as in diphtheria; (2) the allergic manifestation of verrucous endocarditis, and (3) in the septicopyemic type of cardiac complication, a malignant endocarditis. In rheumatism, allergy helps to explain the peculiar picture of the disease. The effects of syphilis and subacute bacterial endocarditis are also discussed.

THE RELATION OF THE ADRENALS TO THE CIRCULATORY COLLAPSE OF DIPHTHERIA. CHARLES W. EDMUNDS and FRANKLIN D. JOHNSTON, Am. Heart J. **4**:16 (Oct.) 1928.

It has been shown that one of the important factors in circulatory collapse of diphtheria is paralysis of the splanchnic nerves, which allows the abdominal vessels to collapse and to act as a reservoir. Also, in severe cases of diphtheria there is toxic parenchymatous myocarditis. It is still a question as to how large a part the myocarditis plays in the failure of circulation since in these cases the heart still maintains a satisfactory circulation if provided with sufficient blood. By experiments on dogs, a lowering in the epinephrine content of the suprarenal gland was determined. This action is probably not specific for diphtheria, but may be explained by the general cachexia. The decrease in epinephrine is probably merely a phenomenon associated with the circulatory collapse.

MANNING, Santa Barbara, Calif.

NERVOUS COMPLICATIONS IN MEASLES. FRANK R. FORD, Bull. Johns Hopkins Hosp. **43**:140, 1928.

Measles is followed by complications referable to the nervous system in about 0.4 per cent of all cases. The author has studied 113 cases described in the literature and adds 12 additional ones. The onset of the nervous symptoms occurs usually on the fourth to the sixth day with drowsiness and convulsions, followed by stupor and accompanied by a sharp secondary rise in temperature. Muscular rigidity and twitchings are typical of this stage; the patient may recover from them promptly without residual symptoms, or they may be succeeded by spastic paralyses, ataxia, tremor, choreic or athetoid movements, myoclonus or aphasia. The spinal fluid, which is almost always under increased pressure, may show an increase in lymphocytes which in one case was as high as 200 cells, and a moderate increase in protein. The pathologic anatomic process is one of toxic degeneration rather than inflammation. A perivascular myelin destruction with collection of lipoid waste products in phagocytes and even in nervous tissue is characteristic. Congestion of the vessels and some increase in glia fibers are also present. These changes are probably not specific for measles. The prognosis for life is good, but residual symptoms are shown in 65 per cent of the patients who survive: weakness, in 30 per cent; ataxia, in 12 per cent; mental defects or change in personality, in 17 per cent, and epilepsy, in 5 per cent.

LESLIE, Evanston, Ill.

VASCULAR OCCLUSION IN DIPHTHERIA. GEORGE D. LYMAN, California & West. Med. **29**:385 (Dec.) 1928.

Vascular occlusion of the limbs is a rare complication of many infectious diseases but is more uncommon in diphtheria than in any of the others; only four cases have been reported in America.

When it occurs in diphtheria, it is usually a complication of the malignant form in which the heart, blood vessels and endocrine glands especially are involved. The complication manifests itself about the fifth or sixth week after the onset and usually in children between 2 and 10 years of age, but apparently not in infancy. It has a predilection for the lower extremities. Most authorities believe that it is caused by an embolus rather than a thrombus. As the signs and symptoms of vascular occlusion occur, the child cries out in anguish from a violent localized pain in one extremity or another, the skin of which will be waxy-white over a considerable extent and will be discolored in irregularly disseminated areas. The patient cannot move the limb and any movement increases the pain. The reflexes disappear, and the pulse is not palpable below the seat of the occlusion. The outcome will be either the sudden death of the patient, increased pain and cyanosis of the limb, which may develop into dry gangrene, or the gradual restoration of circulation in the affected limb, by means of collateral circulation, and a gradual return to a normal condition. The report of a case of the latest condition is given.

JEIDELL, Salt Lake City.

DIPHTHERIA DEATHS IN MASSACHUSETTS, 1927; THIRD CHRONOLOGICAL REPORT. EDWARD A. LANE, New England J. Med. **199**:939 (Nov. 8) 1928.

In 1927, 268 deaths among 4,750 cases of diphtheria were reported in Massachusetts. The fatality rate of 5.6 per cent, approximately one death among every eighteen cases, is the lowest recorded in the state. The mortality rate, 6.3 per 100,000, is the second lowest on record.

A study of 117 investigated deaths from diphtheria showed that the most important cause of death appeared to be the failure of the parents to call a physician at the beginning of the illness. Approximately half of the patients died during the first six days of illness.

Two persons had been given toxin-antitoxin. In one case the treatment had been given for only one month before the illness. The other patient, treated five years before, had not received the Schick test again.

According to the data available, 64 deaths appear to have been the fault of the parents of the patient; 14, the fault of the physician, and 12 that of both parents and physician. In the other 27 instances, either the fault could not be assigned because of insufficient data, or death appeared to be due to an extremely virulent infection. Examples illustrating these various groupings are cited.

GENGENBACH, Denver.

THE PREVALENCE OF COMMUNICABLE DISEASES. Pub. Health Rep. **44**:65 (Jan. 11) 1928.

The epidemic of influenza appears to be traveling eastward with somewhat diminished intensity. If the mortality goes no higher, the outbreak will be classed as of relatively low mortality. The customary seasonal increase was observed in smallpox, meningococcus meningitis, diphtheria, scarlet fever and measles. Typhoid and poliomyelitis showed the normal seasonal decline. There was an increased mortality during the month of November, but the mortality during December was no greater than to be expected for this time of the year.

SANFORD, Chicago.

PARATYPHOID BACILLUS INFECTION WITH PURPURA AND SPECIFIC BRONCHIAL PNEUMONIA. H. P. JAMESON and A. SIGNY, Arch. Dis. Childhood **3**:238 (Oct.) 1928.

In the recent epidemic of paratyphoid fever in London, several children were infected. One unusual case is reported. A girl, aged 8 years, became ill with a headache and vomiting. The following day the feces were loose. On the next day, she had high fever, but other signs were not present. One week later, two or three red spots were noted on the abdomen, but the patient seemed much improved and walked about. Thirteen days after the onset of the infection, a positive Widal reaction was obtained and the child was sent to the hospital. The temperature was irregular. Fifteen days after the onset, purpuric spots were noted on the lip and neck. There was ecchymosis in one conjunctiva followed by hematuria, hemorrhages from the skin and hematemesis. The patient died twenty-five days after the onset. The blood agglutinated *Bacillus parathyphosus B* in a dilution of 1:50,000. Thrombocytopenia was present, the blood platelets being as low as 20,000 per cubic centimeter. A postmortem examination revealed a suppurating pneumonia, confined to one lobe. There were punctate hemorrhages in the pericardium, brain and intestines. Subperitoneal hemorrhages occurred. Pus taken from the infected lung showed *B. paratyphosus B*. Except for the enlargement of several solitary follicles, intestinal lesions were not present.

PETERMAN, Milwaukee.

MUSCLE WEAKNESS, ALTERED GAIT, AND ABSENT DEEP REFLEXES AFTER MEASLES. D. W. WINNICOTT, Proc. Roy. Soc. Med. **21**:1259 (May) 1928.

Muscle weakness, altered gait and absent deep reflexes were reported in a child, aged 6 years, after an attack of measles. There were weakness of the

muscles, absence of tendon reflexes and slight foot drop. Sensory disturbances were not found. The author thought that there must have been a peripheral neuritis. The patient climbed up himself when rising from a lying position on the floor as if he had muscular dystrophy. But against this diagnosis was the fact that the child was definitely improving.

WILLIAMSON, New Orleans.

NASAL DIPHTHERIA IN AN INFANT. G. WITTROK, Arch. Pediat. **1**:36 (Nov.) 1928.

A child, aged 2½ months, did not have a fever or other symptoms except difficulty in breathing and a slight mucosanguineous discharge. Cultures showed Löffler's bacillus. Recovery was rapid following the injection of 3,000 units of antitoxin. The author believes that in difficult breathing in children a few drops of epinephrine should be instilled into the nose; if relief does not follow, diphtheria should be considered. The differential diagnosis should include chronic rhinitis and syphilitic rhinitis.

INFLUENCE OF PUBERTY AND THE EFFECT OF THERAPEUTIC PNEUMOTHORAX ON PULMONARY TUBERCULOSIS IN GIRLS. P. NOBECOURT and J. COLETSOS, Paris méd. **2**:369 (Nov. 3) 1928.

From the study of thirty-four cases of pulmonary tuberculosis in adolescent girls, Nobecourt and Coletsos conclude that the normal evolution of puberty in girls does not seem to favor the development of pulmonary tuberculosis. On the other hand, an abnormal evolution of puberty may or may not favor its development. The authors do not believe that tall young women with a narrow thorax or young women with menorrhagia or metrorrhagia are more susceptible to tuberculosis than are normal young women. They admit the possibility that factory work predisposes children to tuberculosis but emphasize the fact that many cases of tuberculosis develop in school children. Although all these factors play a rôle, there are numerous cases in which, despite the absence of these external influences, pulmonary tuberculosis develops in girls whose puberty has been irregular. Therapeutic pneumothorax gives good results in cases in which the lesions are unilateral; a warning is sounded, however, against affirming prematurely that patients who have improved following the use of this treatment are cured.

SANFORD, Chicago.

GLANDULAR FEVER. J. COMBY, Paris méd. **2**:380 (Nov. 3) 1928.

Comby reports a typical case of glandular fever in an infant, aged 19 months, which occurred during a familial epidemic of influenza. He regards this as most unusual.

SANFORD, Chicago.

THE EFFICACY OF DIPHTHERIA ANTITOXIN WITH SPECIAL ATTENTION TO THE MALIGNANT TYPES OF DIPHTHERIA. G. POLVERINI, Riv. di. clin. pediat. **26**:409, 1928.

The author has tabulated the patients with diphtheria treated at the Milan Contagious Hospital from 1905 to 1927.

The author attributes the fall in percentage of deaths to the larger doses of antitoxin used recently. During 1927, the largest number of cases since 1917 occurred. This epidemic was probably due to virulent organisms as evidenced

	Total Cases			Nasal and Pharyngeal			Laryngeal			Death in Twenty-Four Hours, Cases	Post-diphtherial Paralysis, Cases		Average Dose Antitoxin Units
		Deaths			Deaths			Deaths					
Years	Cases	No.	%	Cases	No.	%	Cases	No.	%		No.	%	
1905-1920	4,881	517	10.6	2,664	197	7.4	2,217	320	14.4	104	241	4.4	8,000
1921-1925	900	77	8.6	565	28	5.0	335	49	14.7	21	55	6.0	12,500
1926-1927	699	55	7.9	501	26	5.1	198	29	14.4	19	52	7.4	18,500
Total	6,480	649	10.0	3,730	251	6.8	2,750	398	14.4	144	348	5.0	

by the high percentage of cases showing paralysis; the diminished mortality is therefore significant. In cases in which the diphtheria is complicated by a streptococcus infection, it is important to give larger doses of antitoxin early. Prophylactic injection of anatoxin (detoxified toxin) is recommended.

Is the Therapeutic Value of Diphtheria Antitoxin in Proportion to Its Content in Immunizing Units? S. Belfanti, Riv. di clin. Pediat. **26**:428, 1928.

The author, who is the director of the Serotherapeutic Institute of Milan, maintains that the efficacy of antidiphtheritic serum is according to its antitoxic properties, and that the current epidemic in Italy with its high mortality was not due to inefficient serum.

Cardiovascular Changes in Children with Malaria. G. A. Piana, Riv. di clin. pediat. **26**:511, 1928.

Cardiovascular effects of malaria may be divided into two groups — subjective disturbances and objective disturbances. The subjective disturbances take the character of anginal attacks, breathlessness and general weakness; the author speaks of these as frequently being real malaria "aura."

The objective disturbance is the enlargement of the heart due to acute myocardial insufficiency, as a result of the malarial toxin. No valvular lesion due to malaria has been observed. The myocardia, which have been injured previously by toxins or infections, are the most easily involved. Disturbances of the cardiac rhythm are usually secondary to myocardial lesions. The arterial pressure is often lowered and the resistance of the vessels diminished.

Typhoid Lymphovaccine and Its Therapeutic Value. G. Taccone, Riv. di clin. pediat. **26**:815, 1928.

Typhoid lymphovaccine is made by adding a culture of Eberth's bacilli suspended in a physiologic solution of sodium chloride to a lymph gland extract. Nineteen children (sixteen with typhoid fever, one with paratyphoid fever and two with both typhoid and paratyphoid fever) were treated by injection of the vaccine, eleven intravenously and nine intramuscularly. The results of the treatment on the whole were favorable, especially in the patients who were treated intravenously. In several cases, the fever subsided after a crisis.

Attempts at Active Immunization Against Chickenpox. Benini Francesco, Riv. di clin. pediat. **26**:824, 1928.

The author reviews the literature on vaccination against chickenpox. He vaccinated 40 children who had been exposed to the disease; of 27 vaccinated by scarification, 7 developed chickenpox, while of the 13 vaccinated intradermally, none developed the disease.

Higgins, Boston.

Measles in Porto Rico. A. F. Isern, Porto Rico Rev. Pub. Health & Trop. Med. **4**:149 (Oct.) 1928.

Measles is a contagious disease of considerable importance in Porto Rico in relation to the mortality which it produces directly or indirectly. It has a biennial periodicity, and aside from its own mortality rate, contributes, to the mortality rate for bronchopneumonia and gastro-enteritis in children less than 2 years of age.

Sanford, Chicago.

Combating Diphtheria in Institutions. G. Knoller, Monatschr. f. Kinderh. **40**:481, 1928.

Describing his attempts to reduce the diphtheria rate in his institution, the author discusses the usual well known methods. After considering them all and

discussing the importance of early diagnosis, the isolation of diphtheria carriers, careful disinfection of the rooms and the use of prophylactic injections of antitoxin, the author concludes that by far the most effective method is the use of the toxin-antitoxin mixture. He recommends it wholeheartedly.

THE PROPHYLAXIS OF CHICKENPOX. L. O. FINKELSTEIN, R. A. WILFAND and E. N. CHOCHOL, Monatschr. f. Kinderh. **40**:489, 1928.

Inoculation of the contents of a chickenpox vesicle into the skin of a normal child gives either an isolated vesicle on the site of the inoculation or, in rare cases, a generalized reaction with an exceedingly mild type of chickenpox. A positive local reaction protects the child from developing chickenpox. The authors do not recommend these inoculations in children who have not been exposed to chickenpox, on account of the danger of contracting the disease.

THE IMPORTANT FACTORS IN THE PATHOGENESIS OF SCARLET FEVER. FELIX VON SZONTAGH, Monatschr. f. Kinderh. **40**:505, 1928.

The author expresses the opinion that the problem of scarlet fever is not yet solved. He alludes to the possibility that a streptococcus is the origin and does not dispute the present theories. He calls attention to the fact that while some members of a family get true scarlet fever, others develop only a sore throat. The difference in reaction cannot be explained on the basis of bacteriology but must be due to differences in the constitution of the patient. Possibly the problem will be solved by studies in the anatomic relations of the lymphoid tissue throughout the throat. At any rate the problem of scarlet fever will not be solved entirely until the constitutional factor is understood.

GERSTLEY, Chicago.

ENLARGEMENT OF THE HEART IN WHOOPING COUGH IN CHILDREN. F. CHAJES-ROSENBUND, Ztschr. f. Kinderh. **46**:55 (July) 1928.

The size of the heart was measured systematically in infants and in small children during pertussis and fifteen months later. In thirty-one children, or 82.6 per cent of the number examined, the heart increased in size during pertussis but, in the majority of cases, returned to normal during the first few months after the cessation of the cough. The change in size occurred in the right auricle and right ventricle. From these investigations, it appeared that neither the age of the child nor the severity of the changes in the rachitic chest influenced the size of the heart. On the other hand, the febrile diseases occurring in conjunction with pertussis, with their increased demand on the circulation, also greatly affected the heart.

VULVOVAGINITIS IN SCARLET FEVER. S. MUSZLINER, Ztschr. f. Kinderh. **46**:156 (July) 1928.

There are few observations in the literature on the occurrence of nonsyphilitic vulvovaginitis with the exanthems of childhood, especially scarlet fever. A causal relation does not exist, as far as the authors can establish. Girls are affected with this disease in almost the same proportion at different ages. The disease is usually mild and from fourteen to twenty-one days in duration.

EMERSON, Boston.

AN EARLY SYMPTOM OF MEASLES. H. JACOBS, Nederl. Tijdschr. v. Geneesk. **72**:3914, 1928.

As a new symptom, which in the author's experience belongs to the morbid picture of measles, he describes a cold, lasting for one day which occurs about a week before the so-called first symptoms of the disease appear, or ten days before the appearance of the exanthems.

Lymphatic Reaction Following Chickenpox. A. van Westrienen, Nederl. Tijdschr. v. Geneesk. **72**:4015, 1928.

In this article a lymphatic reaction after chickenpox is described in a girl, aged 6 years. The case was peculiar on the following grounds:

1. The lymph glands were affected to a slight degree and only in the later stage. The enlargement of the liver was great and lasted much longer than the enlargement of the spleen.

2. After a fairly long period (four weeks) in which the eosinophil cells were totally absent, a strong eosinophilia developed (up to 13.5 per cent).

3. The lymphatic reaction appeared after the girl recovered from chickenpox. The author could not find another example of this.

Five months after the recovery from chickenpox, when the blood picture had become about normal, with the exception of a slight lymphocytosis, the patient was admitted to the hospital because of scarlatina. After this second infectious disease the lymphocytosis disappeared totally, and a lymphatic reaction did not occur.

The author discusses which of the two explanations of the cause of a lymphatic reaction, found in the literature, should be given in this case. A positive answer cannot be given. As is normal in chickenpox, the lymphatic system reacts most; in this case it is certain that a specific reaction resulted from a specific stimulation, though this reaction was abnormal in regard to its intensity and duration. But whether with this a pathologic constitution also played a rôle cannot yet be decided.

Van Creveld, Amsterdam.

A New Method of Treating Tetanus. Sladky, Čas. lék. česk. **65**:141 (Jan.) 1926.

The author performed spinal anesthesia with 10 per cent tropacocain after several intravenous injections of magnesium sulphate which gave no reaction. The spinal injection produced a cessation of all painful convulsions except the trismus and overcame the dyspnea and the almost unbearable motor and sensory stimulation. The trismus was controlled by an injection of 0.5 per cent Braun's solution directly into the masseter muscles. The patient then was able to eat and swallow. The author feels that a moribund boy, aged 11 years, was saved by the injection of 10 cc. of the before-mentioned solution. Antitetanic serum was used during the early part of the treatment.

Stulik, Chicago.

The Types of Dysentery Bacilli and the Prognosis of Dysentery in Children in Dairen. T. Yoshitomi, Orient. J. Dis. Inf. **2**:133, 1927.

The figures for 1925 are presented.

Type of Bacilli	Number	Average Duration of Illness	Mortality
Flexner	19	25 days	2 (8%)
Shiga	5	33 days	
Y	26	22 days	6 (23%)

Dysentery in Children; Epidemics in Families. N. Hoshi, Orient. J. Dis. Inf. **2**:134, 1927.

Thirty-six cases were observed in which two children in a family had dysentery. In fourteen instances, two brothers had the disease; in twelve, two sisters; in ten, an older sister and a younger brother; in none, an older brother and younger sister.

The fever tended to be higher in the older child, but did not last so long as in the younger. The older children showed more anorexia and vomiting. The younger children showed more marked intoxication and diarrhea and also more frequent complications, such as pneumonia, in the ratio of 50:22 per cent.

The mortality among the younger children was 22 per cent; among the older 11 per cent. The older children showed the higher agglutination titer of blood serum to the dysentery bacilli.

THE THERAPEUTIC RESULTS AND THE CHANGE IN THE BLOOD PICTURE IN WHOOPING COUGH AFTER ROENTGEN TREATMENTS. T. SUZUKI and S. KAWASHIMA, Orient. J. Dis. Inf. **3**:9, 1928.

Roentgen treatment for whooping cough caused a diminution in the number of paroxysms, in the size of the hilum glands and in the number of lymphocytes in the blood.

CHEMICAL ANALYSIS OF THE BACILLI OF WHOOPING COUGH. M. FUKUSHIMA, Orient. J. Dis. Inf. **3**:14, 1928.

Analysis of the pertussis bacilli showed from 70 to 80 per cent of water and from 20 to 30 per cent of solid material of which 8.04 per cent is lipoid. The protein content of the bacilli is 11.46 per cent. Other bacteria similarly analyzed showed the following content:

	Lipoid, Per Cent	Protein, Per Cent
Pneumococci	3.4	17.6
Bacillus diphtheriae	2.1	4.2
Staphylococcus aureus	1.5	7.5
Staphylococcus citreus	1.0	...
Staphylococcus albus	1.5	7.8
Bacillus pyocyaneus	1.7	...
Micrococcus catarrhalis	3.2	6.1
Bacillus dysenteriae	1.5	...
Bacillus typhosus	1.3	...
Bacillus paratyphosus	1.0	...

The bacilli living in the respiratory tract are rich in lipoid material, while those living in the intestine are poor in lipoid material. The protein contents of *B. pertussis* and the pneumococcus are high.

EXPERIMENTAL STUDIES OF THE LYMPHOCYTOSIS OF WHOOPING COUGH MENINGITIS. M. FUKUSHIMA, Orient. J. Dis. Inf. **3**:15, 1928.

The author made intraspinal injections of (*a*) *Bacillus pertussis*, (*b*) lipoid substance of *B. pertussis*, (*c*) *B. pertussis* minus lipoid and (*d*) an aqueous solution of the protein of *B. pertussis* into rabbits. Twenty-four hours later, the spinal fluid was examined. In *a* and *b* lymphocytes prevailed, while in *c* and *d* polymorphonuclear leukocytes were predominant. Lymphocytes were found consuming particles of lipoid substance. Thus the lipoid component of the pertussis bacilli has power to cause lymphocytosis. The pertussis bacillus has previously been shown to be rich in lipoid material. The author suggests that a lipotoxin is responsible for the lymphocytosis in whooping cough meningitis.

EXPERIMENTAL STUDIES ON THE LYMPHOCYTOSIS OF WHOOPING COUGH: III. M. FUKUSHIMA, Orient. J. Dis. Inf. **3**:43, 1928.

Injection of the killed pertussis bacilli or of the lipoid component (ether extract) of the pertussis bacilli into rabbits caused a marked leukocytosis with relative lymphocytosis. Injection of the lipoid-free component of the same bacilli caused a marked leukocytosis, but the number of lymphocytes was diminished.

The author concluded that the lymphocytosis of whooping cough is explained by the action of the lipoid component of the bacilli.

HIGGINS, Boston.

Chronic Infections

TUBERCULOSIS IN INFANTS AND YOUNG CHILDREN. LLOYD B. DICKEY, California & West. Med. **29**:388 (Dec.) 1928.

Many infants become infected with tuberculosis without showing sign of serious tuberculous disease. Asserson's study of 4,003 infants less than 2 years of age, in hospitals and clinics and of 1,656 infants of the same age attending health centers, indicates that the resistance of the infant to tuberculous infection, although relatively low, is greater than was formerly believed. The study also indicates that tuberculous infection in infancy is usually a matter of continued exposure.

During the course of work done under the auspices of the San Francisco Tuberculosis Association, in which tuberculin tests were given regardless of complaint, positive reactions were frequently seen without symptoms referable to tuberculosis. Most of the patients whom it was possible to follow did not develop symptoms afterward. When a positive reaction was obtained, a complete history was secured, with special reference to tuberculosis, and a complete physical examination, and roentgenologic and fluoroscopic studies were made. The cases in which there were symptoms or physical signs in addition to roentgenologic evidence of the disease were called active; those without symptoms or signs, but with what might be roentgenographic evidence of tuberculous disease, were classified as cases of suspected tuberculosis; those without signs or symptoms and in which roentgenograms showed definite calcifications were classified as healed. Seven hundred and thirty-eight children, less than 4 years of age, were tested and 105 were positive reactors. Of these 105, in 24 the disease was active, in 29 suspected, in 46 healed and in 6 not classified due to incomplete histories.

At the present time, from three months to two and one-half years after they were first seen, 17 of the 24 patients with the active form of the disease are living, 4 are dead and 3 have disappeared from observation. Of the 17 living, 9 are free from disease, 3 are at home ill with symptoms of tuberculosis and 5 are in hospitals for tuberculous patients. Of the 29 patients classed as having suspected tuberculosis, 1 is dead, 2 are ill with symptoms of tuberculosis, 3 have disappeared and 23 are well. Of the 46 patients in whom the disease was healed, one has disappeared from observation, and the other 45 are well.

The author concludes that: 1. Tuberculous infection is fairly common in infancy and early childhood. 2. In the absence of symptoms and roentgen observations, these patients usually do not develop pronounced evidence of the disease. 3. Occasionally, patients with marked evidence of disease may carry the disease for a considerable time without any increase of signs or symptoms. 4. Seventy-seven per cent of children less than 4 years of age, in this series, that reacted positively to tuberculin tests did not develop evidence of tuberculous disease. 5. The intracutaneous test and the roentgen ray are the most valuable aids in diagnosis.

JEIDELL, Salt Lake City.

INTRATRACHEAL EVACUATION OF A TUBERCULOUS GLAND: DEATH BY ASPHYXIA. E. PICHON and MLLE. CATHIER, Bull. Soc. de pédiat. de Paris **9**:441 (Nov.) 1928.

A child, aged 2½ years, suddenly developed severe inspiratory and expiratory stridor which were not benefited by intubation. It died of asphyxia. Autopsy showed a caseous mass obstructing the trachea just above the bifurcation; the mass was found to have originated from a ruptured tuberculous gland.

SUPPURATIVE CERVICAL ADENITIS IN AN INFANT GIVEN B.C.G. LEON TIXIER, Bull. Soc. de pédiat. de Paris **9**:447 (Nov.) 1928.

A girl, aged 20 months, who was the second child born of nontuberculous parents and who had been given B.C.G., developed suppurative cervical adenitis; the other child did not receive B.C.G., and remained well. The author attributes the suppurative adenitis to the vaccination. The adenitis appeared to him to be tuberculous, but he made no inoculations in animals or other tests to prove it to be such. He advises against the use of B.C.G. in infants who are not likely to live in a tuberculous environment.

THE RESULTS OF A SURVEY OF CHILDREN VACCINATED WITH B.C.G. DURING 1926 AT THE MATÉRNITÉ DE L'HÔPITAL BOUCICAUT. M. LELORIER, Bull. Soc. de pédiat. de Paris **9**:455 (Nov.) 1928.

Of 742 infants who received B.C.G. during the year 1926 at this matérnité, 459 were followed. The mortality during the period from eighteen to thirty months after the vaccination was 10.3 per cent; whereas, in 1926, the mortality

in the first year of life of all infants in Paris was 9.7 per cent, and in the suburbs, 12.2 per cent. Details are given regarding the environment and health of the groups studied, but not about infants who were not vaccinated.

CLAUSEN, Rochester.

THE SUDDEN DEATH OF AN INFANT BORN OF A TUBERCULOUS MOTHER AND GIVEN B.C.G. LEON and F. VIOLA TIXIER, Bull. Soc. de pédiat. de Paris **9**:450 (Nov.) 1928.

The mother, apparently suffering from active tuberculosis, had one child three years previously which did not receive B.C.G., and which remained well. The next infant received B.C.G. in the usual doses on the third, fifth and seventh days. On the fourteenth day, profuse diarrhea appeared, leading to rapid dehydration and death. No autopsy was performed. This infant had never been in contact with the mother. The other fourteen infants in the same nursery had not been ill although all had received B.C.G. The mothers of none of these were tuberculous. The author feels that he can exclude diet and acute infection as a cause of diarrhea in this case, and warns against administering B.C.G. to infants whose mothers have active tuberculosis. He cites the similar experience of others.

A CASE OF UNUSUAL PRIMARY SYPHILIS. W. RIBIERO, Arch. Pediat. **1**:32 (Nov.) 1928.

Ribiero's patient was a boy, aged 12 years, who entered the clinic with a typical primary syphilitic lesion on the lip. There was a direct history of exposure, ten days before. The lesion disappeared and, after arsenical treatment, the Wassermann test gave a negative reaction.

SANFORD, Chicago.

SYPHILITIC ANEMIA OF EARLY INFANCY. ALFREDO CASAUBON and JOSÉ DELUCCHI, Arch. latino-am. de pediat. **22**:613, 1928.

The authors do not believe that syphilis in the infant produces a specific, constant, and characteristic blood picture. The blood formula depends on the age of the child and the virulence of the infection, and also on the previous state of the hematopoietic system.

There may be abnormal vulnerability or predisposition of the blood system in these infants which causes them to react with grave forms of disease of the blood to even light attacks of the infection. Other contributing factors, aside from the disease itself, are prolonged lactation, superadded infections, and defective hygienic conditions.

SCHLUTZ, Minneapolis.

SPASTIC HEMIPLEGIA AND CONGENITAL SYPHILIS IN CHILDHOOD. V. MIKULOWSKI, Riv. di clin. pediat. **26**:809, 1928.

A case of hemiplegia in a child aged 2 years is reported. A diagnosis of congenital syphilis involving the cerebral vessels was made by the clinician and confirmed at necropsy.

HIGGINS, Boston.

THE EARLY DIAGNOSIS AND TREATMENT OF SYPHILIS IN MOTHER AND CHILD AS A PROBLEM IN SOCIAL HYGIENE. W. ERNST, Ztschr. f. Geburtsh. u. Gynäk. **93**:443, 1928.

The author stresses the important and strategic position which the obstetrician occupies in making a diagnosis of and instituting treatment for syphilis. He states that about 6 per cent of the pregnant women in Stoeckel's clinic at Berlin have active syphilis. Infection of the fetus takes place about the fourth or fifth month of pregnancy. As a result, the termination of pregnancy during the first four months because of syphilis is unusual.

The author agrees with Boas and Gammeltoft and Nuernberger that at least 95 per cent of the infants born to syphilitic mothers develop syphilis.

The infants of mothers treated before pregnancy have a better outlook; 22 per cent remain healthy. The prognosis is even better when the mother is treated during pregnancy, as about 88 per cent of these infants are born healthy. When the mother is given antisyphilitic treatment both before and during pregnancy, the infant has an even better chance.

The method of diagnosing maternal syphilis is not simple. Nonsyphilitic serum reactions occur in from 5 to 6 per cent of pregnant women. The author uses three types of reactions: Wassermann, Sachs-Klopstock and Meinicke. The last rarely gives a nonsyphilitic reaction. If two tests give positive results, syphilis is probably present. The history and observations are of great importance but not always available. In case of doubt, the tests are repeated.

About 80 per cent of syphilitic newly born infants give negative reactions serologically. It is possible to find the living spirochete in tissue fluid obtained from the fetal end of the cord, by using dark field illumination.

The use of roentgenograms of the fetal skeleton is also important. The diagnosis may of course be made from physical examinations. The diagnosis should be certain and treatment instituted.

The women must come to the clinic early in pregnancy, and the serodiagnosis should be a routine procedure. The syphilitic mothers and infants must be systematically followed up and treated. Syphilitic women should be advised of the necessity of treatment in case of subsequent pregnancy.

ADAIR, Minneapolis.

THE CLINICAL HEMATOLOGY OF INFANTS: VIII. CONGENITAL SYPHILIS AND PNEUMONIA. E. STRANSKY, Ztschr. f. Kinderh. **46**:23 (July) 1928.

During the first weeks of life, continued illness sometimes causes severe anemias, for the most part characterized by more or less embryonic blood pictures corresponding to the centers for blood formation in the liver, spleen, kidneys and lymph glands. An exception was described earlier, a severe anemia without signs of regeneration. The course of the disease is severe and always progresses with severe general syphilis. In the course of the anemia, symptomatic hemorrhages are frequent. Later in infancy, the anemias, as far as they have been observed, are caused not only by syphilis, but by other infections which occur frequently in the infants affected with congenital syphilis. The prognosis of these anemias is far more favorable if, on account of their origin, antisyphilitic treatment is not the only kind given.

EMERSON, Boston.

ACUTE TUBERCULOUS SEPSIS. J. PELNAR, Čas. lék. česk. **65**:12 (Jan.) 1926.

The author describes sepsis in a boy, aged 12 years, that has the clinical picture of typhoid. The observations, however, show 8,000 white blood cells, a negative Widal reaction, no roseola, a small spleen and liver, positive D'Espine's sign and a positive Mantoux reaction (1:10,000). The probable pathogenesis is primary infantile infection from the mother, a latent mediastinal tuberculosis, breaking through as a tuberculous pleurisy when the child was 10 years of age, now resulting in septicemia. Systemic associated factors in the activation of latent tuberculosis are measles, pertussis, and chickenpox. The prognosis of tuberculous sepsis is not as poor as that of miliary tuberculosis. The prognosis of acute tuberculosis of the new-born infant is 11 per cent in families with a history of tuberculosis and 55 per cent in nontuberculous families. The treatment for the sepsis is essentially hygienicodietetic.

STULIK, Chicago.

Internal Diseases

THE ROENTGENOLOGIC DIAGNOSIS OF LIVER ABSCESS WITH OR WITHOUT SUBDIAPHRAGMATIC ABSCESS. HENRY K. PANCOAST, Am. J. Roentgenol. **16**:303 (Oct.) 1926.

The essential points in diagnosis are: a correct clinical history, knowledge of the pathology of the abscess, a roentgenoscopic study of diaphragmatic move-

ment, and knowledge of the differential diagnosis and the roentgen observations, which include (1) elevation of the dome of the diaphragm, (2) restricted movement of the diaphragm, (3) absence of supradiaphragmatic symptoms, except a reaction or a slight effusion of the lung and (4) the exclusion of subdiaphragmatic conditions such as operative trauma, nonsuppurative cholangeitis, perirenal abscess, acute peritonitis, hepatic gumma, hepatic hydatid cyst and amebic abscess.

STULIK, Chicago.

THE CHEMICAL ANALYSIS OF LIVER AND SPLEEN FROM A CASE OF LIPOID HISTIOCYTOSIS. R. P. MACFATE, Arch. Path. **6**:1054 (Dec.) 1928.

The liver and spleen from a patient with Nieman-Pick's disease showed a great increase over the normal lipoid content, especially phosphatids. This observation confirms previous work. The analysis serves to confirm the differentiation between Gaucher's disease and Niemann-Pick's disease, the latter having the greatest deposition of phosphatids, cholesterol and cholesterol esters, of which the phosphatids predominate, and showing the absence of any considerable quantity of kerasin. Lipemia and hypercholesterolemia are present in persons with Niemann-Pick's disease.

SANFORD, Chicago.

BACILLUS COLI NEPHRITIS. WALTER BROADBENT, Practitioner **121**:26, 1928.

Bacillus coli nephritis or pyelonephritis is much commoner than used to be thought. It occurs frequently in infants and young children, nearly always girls.

The onset may be acute, with rigors, vomiting and pyrexia of from 102 to 104 F. Renal pain as well as rigidness and tenderness of the abdomen may be present. In the differential diagnosis, influenza, malaria and stone must be considered.

Treatment consists of rest in bed, warmth and free administration of water and alkalis.

In chronic cases, alternating alkali and acid hexamine mixture is beneficial. Hexylresorcinol is useful in getting rid of *Bacillus coli*.

THE DIAGNOSIS AND TREATMENT OF CHRONIC INTESTINAL STASIS IN CHILDREN. A. GRAHAM STEWART, Practitioner **121**:183, 1928.

The condition is common and is the result of wrong diet and wrong habits. The child looks pale and pasty with baggy eyes, and the eye itself is dull. The abdominal muscles are flabby, and the skin of the abdomen and flanks is a dirty brown. Developmental failure is general, and spinal curvature and flatfoot are often present. The elbow joints are overextensible, and the upper part of the back is covered by downy hair. Venous peripheral stasis is common; cold extremities, a mottled leg and glandular enlargements are found, and the child is subject to recurring bronchial attacks and mild pyrexia in the evening.

These children are liable to repeated attacks of acidosis. They fail to gain in weight and are a source of continual anxiety. They are constipated, even though they have one regular movement a day, and the colon is never empty. Bacterial examination of the feces confirms the diagnosis, and the x-rays may reveal one of the following conditions: an elongated pelvic colon, a diseased appendix, Lane's kink, stasis in the large intestine, sacculation and spasm at the ileocecal valve, torsion acting as a kink and loose adhesions.

If there is a diseased appendix or a kink, operation must be resorted to.

Medical treatment consists of rest, roughage in the diet, abdominal massage and mechanical support. Vaccines with streptococcus infections and a squatting position for defecations are advocated. The foot of the bed should be raised 6 inches. Colonic lavage should be instituted.

The bowels must be made to move twice a day, and laxatives may be used at first and omitted as soon as possible.

GELSTON, San Francisco.

DOUBLE AORTIC ARCH AND PULMONARY ATRESIA, WITH THE PULMONIC CIRCULATION MAINTAINED THROUGH A PERSISTENT LEFT AORTIC ROOT. DIGBY WHEELER and MAUDE E. ABBOTT, Canad. M. A. J. **19**:297, 1928.

A case of a rare congenital cardiac anomaly in a man of 29 years is described, with its clinical history and postmortem and anatomic observations. The following cardiac anomalies were found:

1. An incomplete double aortic arch, the intermediate portion of the left arch being deficient.
2. Dextroposition of the aorta.
3. Pulmonary atresia.
4. The ductus arteriosus persisting as a small vessel which communicates only with the hilum of the right lung through the right pulmonary artery.
5. Pulmonic circulation maintained by means of hypertrophied bronchials, branches of the left aortic root.
6. An incomplete ventricular septum, the endocardial cushions having failed to fuse.

MOORE, Omaha.

HEREDITY IN EXOPHTHALMIC GOITER. E. A. COCKAYNE, Arch. Dis. Childhood **3**:227 (Oct.) 1928.

All members of a family which consisted of five females and three males were healthy. The oldest of the daughters had two children. One of these who was normal had two children, the first a normal boy and the second a girl, aged 8 years, who had exophthalmic goiter. The second daughter of the first generation had a son and a daughter. The son was apparently normal, but his only child had a severe form of exophthalmic goiter. Since both father and son had lived in Canada for many years, the factor of environment was ruled out. The third daughter, or the aunt of the boy with Grave's disease, developed Grave's disease at the age of 24, but had two healthy children.

The author reviews some of the reported instances of heredity in exophthalmic goiter and is of the opinion that the inheritance may be explained on the mendelian theory. The constitutional weakness of the gland is inherited as a dominant. Some of those who inherit this characteristic remain normal; others present any or all the symptoms.

PYELITIS COMPLICATED BY JAUNDICE. E. GÖRTER and G. O. E. LIGNAC, Arch. Dis. Childhood **3**:232 (Oct.) 1928.

Three cases of pyelitis with jaundice are reported. The first case was considered *Bacillus coli* septicemia. In the second which was called a typical mild case of pyelitis, the blood contained 20 mg. of bilirubin per liter. The van den Bergh direct reaction was negative. The third was rather a severe case of pyuria with jaundice. The authors review the literature and then describe the autopsy in the first case, a boy aged 4 months. The following positive conditions were noted: a saffron colored skin and intensely jaundiced sclerae, and an intense yellow color of the subcutaneous fat. The endocardium and the lungs were also stained yellow. The liver was of a diffuse green, resulting in a diagnosis of cholangitis. The kidneys were large, weighing 125 Gm., and mucous yellow matter was found in the pelvis. A thin, yellow membrane covered the pyramids and the mucous membrane of the calices. Microscopically, these membranes were found to be fibrin and desquamated epithelium. The color of the cortex of the kidney was grayish yellow with yellow patches. On a pathologic basis, a diagnosis was made of fibrinous pyelitis and cellular pyelonephritis.

A BLOOD FAT CELIAC DISEASE. A. MONCRIEFF and W. W. PAYNE, Arch. Dis. Childhood **3**:257 (Oct.) 1928.

These authors accept the following definition of celiac disease given by R. Miller: "A digestive disorder arising in infants and young children who show

no evidence of chronic intestinal or other organic abdominal diseases. It is characterized by a persistent malabsorption of dietetic fat which causes large stools containing an excess of split fat, enlargement of the abdomen, lack of growth and other symptoms." Two cases are reported which presented many points of similarity to the celiac diseases; these patients had the typical stools. At autopsy, one case was found to be of tuberculous peritonitis; in the other, a definite diagnosis was not made. It is assumed that the fat in the feces is normally split and that the intestinal ferments are present normally. The lacteals are not obstructed. Absorption of the fat seems to be attained experimentally in celiac diseases. The fat represents some form of excretion from the intestinal tract. The primary fault in celiac disease is a malutilization and not a malabsorption of fat; it is a defect of fat metabolism analogous to the defective utilization of sugar in diabetes. The estimations of blood fat on five normal controls and in six probable cases of celiac disease are presented. The fatty acid in the blood was found to exist in a much greater amount in five of the cases of celiac disease.

PETERMAN, Milwaukee.

PNEUMONIA IN YOUNG INFANTS WITH A DEVIATION OF THE HEART TOWARD THE SIDE OF THE LESION. A. G. MAITLAND JONES, Proc. Roy. Soc. Med. **21**:1327, 1928.

The author reports three cases in full, including, in one case, a report of the postmortem examination.

WILLIAMSON, New Orleans.

ESSENTIAL PAROXYSMAL TACHYCARDIA: TREATMENT. E. PICHON, HABERT and MLLE. KRITCHEVSKY, Bull. Soc. de pédiat de Paris **9**:442 (Nov.) 1928.

Polonovski and Nitzberg have recently isolated from the calabar bean an aminoxide which is said to act as a vagal stimulant and sympathetic sedative. The action resembles that of physostigmine, but is more prolonged, and the toxic effects are less. Pichon administered the drug by mouth in doses of 0.5 mg. b. d. to a boy, aged 13 years, who had suffered since the age of 5 years with attacks of paroxysmal tachycardia which gradually increased in frequency and in severity. Relief from symptoms was quickly afforded in the two attacks observed.

CLAUSEN, Rochester.

INTRADERMAL TESTS WITH PEPTONE AND COLON BACILLUS FILTRATE. A. B. MARFAN and S. DREYFUS, Nourrisson **16**:236 (July) 1928.

Intradermal tests were made on a group of infants suffering from intestinal disorders, with a series of ten normal infants used as controls. The results were so discordant that conclusions of value could not be drawn.

MCCLELLAND, Cleveland.

ACROCYANOSIS OF PERMANENT TYPE IN YOUNG SUBJECTS. J. COMBY, Arch. de méd. d. enf. **31**:645, 1928.

Under the term of acrocyanosis, Comby discusses a specific cutaneous condition characterized by cyanosis of the hands, the feet, often of the ears, nose and lips and accompanied by algidity, appearing in young persons about the age of puberty. Once established, it continues into adult life and on to old age; it is commonly associated with hyperhidrosis and has been described under various titles such as the submalleolar hypostatic cyanosis of Delater and Hugel. Four times as many cases are found among girls as among boys. Its etiology is so obscure that it may well be considered an evolutionary disease, with such factors as cold, humidity and emotional disturbances acting only as exciting agents. Heredity assumes an important rôle in its etiology, the parents frequently showing neuro-arthritic manifestations.

The pathology is likewise a source of controversy. The condition may be due to an irritation of the neurovegetative apparatus or it may be caused by an endocrine insufficiency, particularly of the suprarenals, the intimate relation of which with the sympathetic system is admitted by all clinicians. The symptoms are those which would naturally follow extreme congestion in the capillary circulation of the extremities — cold hands and feet, excessive perspiration and in winter, chilblains and chapped skin. The fingers and toes are swollen to the point of deformity and vary in color from extreme lividity to a vinous hue. In aggravated cases the face is involved, the nose then assuming the appearance of granulosis rubra nasi. All of these subjects are of the nervous type: emotional, unstable and timid. Psychasthenia is common. Treatment is ineffective.

AMESSE, Denver.

INFANTILE SPLENIC ANEMIA OF THE FAMILIAL TYPE. A. MACCANTI, Riv. di clin. pediat. **26**:620, 1928.

Seven cases of splenic anemia occurring in children are reported. Five of the children were from 6 to 8 months of age, one 11 months and one 2 years. The cases were characterized by enlarged spleens, anemia and nucleated red cells.

One child had three brothers and sisters, two of whom died of a similar type of anemia when 19 and 39 months of age. Another child had two sisters, one of whom died of severe anemia when 9 months of age.

HIGGINS, Boston.

ARTIFICIAL PNEUMOTHORAX IN THE TREATMENT OF PNEUMONIA IN CHILDREN. J. IBRAHIM and J. DUKEN, Arch. f. Kinderh. **84**:241 (July 20) 1928.

An infant, aged 10 months, suffered from bronchopneumonia with an interlobar exudate and high fever. Pneumothorax occurred after about fourteen days; immediately afterward, the fever was reduced and the patient began to recover. These results led the authors to believe that artificial pneumothorax might be employed therapeutically in similar cases. In the two cases reported, the treatment was used successfully. One was a case of interlobar pleurisy with pneumonic foci in the upper right lobe of the lung in a boy, aged 1½ years, and the other, a case of pneumonia in the upper right lobe of the lung in a girl, aged 2 years. The authors do not suggest that this method be used in the majority of cases of pneumonia in children, for its application is limited. It is contraindicated in cases showing extensive bilateral pneumonic processes, whether acute or chronic; in unilateral pneumonic disease when severe bronchitic symptoms are present in both lungs, and in cases showing indurated adhesions. It is to be employed when conservative treatment fails in pneumonia that is localized in one lung (whether complicated or not by interlobar exudate), especially when there is danger that bronchiectasis may develop.

LITHIASIS IN INFANCY. O. ULMER, Arch. f. Kinderh. **85**:87 (Sept. 28) 1928.

Ulmer presents a case of lithiasis, with roentgenograms, in a child, aged 22 months. In a review of the literature, it was noted that in 1,836 cases, there were 1,319 of urinary calculi, 508 of urethral stone, and 9 of renal calculi. The colloidal and hereditary factors in the etiology are discussed.

A FAMILIAL OCCURRENCE OF POLYROSPASM. A. BRATUSCH-MARRAIN, Arch. f. Kinderh. **85**:93 (Sept. 28) 1928.

Pylorospasm was observed in three children in one family. The mother gave a history of nervousness and vomiting. At the age of 4 weeks, the first child had projectile vomiting and peristaltic waves. Following indifferent success with atropine, an operation was performed and a small tumor of the pylorus was found. A year later, this child's brother, aged 5 weeks, presented the same symptoms,

and at operation hypertrophy of the pyloric musculature was found. Three years later another brother, aged 2 months, came to the clinic with the same symptoms. Peristalic waves were observed, but a tumor was not found. This child recovered under atropine therapy without an operation.

SANFORD, Chicago.

THE REACTION OF JUVENILE DIABETES INSIPIDUS TO EXTRACTS OF THE HYPOPHYSIS. EMILIE WEISS, Monatschr. f. Kinderh. **40**:428, 1928.

In an excellent study, the author experimented with nine pharmaceutical preparations of the hypophysis. Of them all she found the pituitary of Parke, Davis and Company by far the most effective in diminishing the quantity of urine and the thirst, and in increasing the specific gravity of the urine. Writers have found that other preparations are effective in adults. The author does not explain the difference in results other than by the suggestion that children react differently than adults to various remedies.

GERSTLEY, Chicago.

THE TREATMENT OF DIABETES WITH INSULIN. LEO HERMANNS, München. med. Wchnschr. **75**:2168, 1928.

Every method used in treating a patient for diabetes must have as its object arrangement of the diet so as to spare and save the pancreas as early as possible (Naunyn). The production of insulin begins only when the sugar in the blood provides the irritant (Staub). If the amount of blood sugar is kept down to the normal level, the pancreas is saved. The author's method is to keep the blood sugar at the normal level. The glycemic reaction is not only dependent on the condition of the pancreas and liver but also on the influence of the sympathetic nervous system and certain endocrines. The diabetic patient has a less labile control of blood sugar content. In a discussion of methods of caring for the diabetic patient, the author states that Allen's original method has only historical interest.

At first, the author uses Pétren's diet for from one to two days. This consists of from 200 to 250 Gm. of fat in the form of bacon and butter, and from 600 to 1,000 Gm. of vegetables; later fruit, cream, coffee, tea and broth are given. Thus, proteins are excluded as far as possible.

Next there is a fasting period for two days, following Allen's method. Only liquids are given. At this time, six injections of from two to three units of insulin are given at two hour intervals.

In the third period, fat and vegetables are given, with sufficient insulin at two to three hour intervals to keep the blood sugar at the normal level.

During the final period the patient is given from 20 to 25 calories per kilogram of weight: 1 Gm. of protein per kilogram and as much carbohydrate as will not raise the amount of blood sugar above the normal level so that it becomes irritating to the pancreas.

The author considers that this method is not a cure for diabetes, but that maintaining the normal amount of blood sugar is a physiologic cure.

SCHORER, Kansas City, Mo.

THE CLINICAL HEMATOLOGY OF INFANTS: VII. BLOOD CHANGES IN PYURIA. E. STRANSKY, Ztschr. f. Kinderh. **46**:13 (July) 1928.

Beginning pyuria is always characterized by a shifting to the left of the neutrophilic picture and usually by a leukocytosis and an increase in the number of neutrophils. If the pyuria lasts longer, anemia develops, which varies in grade from that of a simple secondary anemia to that of the Jaksch-Hayem symptom-complex. In chronic pyuria, blood transfusion causes not only a disappearance of the anemia, but recovery from the pyuria itself.

THE TREATMENT OF DIABETES MELLITUS IN CHILDREN. R. PRIESEL and R. WAGNER, Ztschr. f. Kinderh. **46**:62 (July) 1928.

In order that the diet may be complete for diabetic patients, it must be: (1) consistent with the diabetic metabolism, (2) beneficial to the patient, (3) reconcilable with the smallest possible amount of insulin, (4) borne without disturbance of the hypoglycemic episodes for long periods of time, (5) suitable for home management and (6) physiologic as measured by the growth and development of the child, but not by the mutual correlation of protein, fat and carbohydrate. The term "physiologic" presupposes also a healthful minimum of protein as well as a corresponding content of salt and vitamin.

PRETERNATURAL SOFTNESS OF THE YOUNG SKELETAL SYSTEM: I. LATE RICKETS AND OSTEODYSTROPHIA FIBROSA. J. DUKEN, Ztschr. f. Kinderh. **46**:114 (July) 1928.

The disease picture of osteodystrophia fibrosa, isolated or combined with late rickets is especially interesting from the point of view of therapeusis. The observations of the authors, like those in the literature, show that rickets apparently is caused by some disturbance of the endocrine glands. On this assumption, it must not be considered that all forms of rickets are nosologically the same; instead, the contrary is implied in this and previous communications.

PRETERNATURAL SOFTNESS OF THE YOUNG SKELETAL SYSTEM: II. LATE RICKETS, TETANY AND CHRONIC CONTRACTED KIDNEYS (RENAL RICKETS). J. DUKEN, Ztschr. f. Kinderh. **46**:137 (July) 1928.

According to this and the previous communication, rickets cannot be regarded in general as an avitaminosis; further rickets may become completely healed, even when marked acidosis is present. The onset of tetany must depend conditionally on an alkalosis and likewise on a sinking of the quotient $\frac{Ca}{P}$ to the value of 1.2. These established facts must mean that neither rickets nor tetany in general can be expressed by a short formula and that for the present the whole process must appear as extraordinarily complicated.

EMERSON, Boston.

HODGKIN'S DISEASE IN AN INFANT. C. W. HERLITZ and F. WAHLGREN, Acta paediat. **8**:218 (Aug. 15) 1928.

Enlargement of the cervical gland commenced in an infant at the age of 5 months. The patient was admitted to the hospital when he was 8 months old, and the diagnosis was confirmed at that time by the excision of a lymph node. Various therapeutic measures were attempted, including ultraviolet irradiation and radiotherapy, but the patient died at the age of 18 months. Detailed clinical notes and an autopsy protocol are given.

MCINTOSH, Baltimore.

INSULIN AS AN AID FOR INCREASING WEIGHT. SIGGAARD ANDERSEN, Ugesk. f. Laeger **90**:1013, 1928.

Seven cases are presented showing marked increase in weight during insulin therapy. The duration of treatment was from two to five months, and the minimum to maximum gain was from 6 to 17 Kg.

Four of the seven patients were 20 years of age or less. The general symptoms presented were anorexia, emaciation, gastric hypotonicity and dyspepsia.

A discussion of the scientific basis for the action of insulin is also presented. The fact that the respiratory quotient rises to 1.1 is evidence of increased conversion of carbohydrates into fat. There is also some evidence that the lowering in the amount of blood sugar increases hunger. This, however, was not a constant observation.

The contraindications for the giving of insulin to nondiabetic patients are mentioned. A cachectic patient or one suffering from a febrile tuberculous condition should not be given insulin.

The technic of administration is outlined. A test dose of 8 units given subcutaneously three times a day, one-half hour before meals is fairly safe. This dosage may be gradually increased. The highest dose used was 32 units three times a day. Symptoms of hypoglycemia are treated as in diabetes.

SCHLUTZ, Minneapolis.

STATISTICS IN TWO HUNDRED AND NINETY-EIGHT CASES OF LEAD POISONING IN INFANTS. M. FUKUSHIMA and H. MATSUMOTO, Orient. J. Dis. Inf. **3**:27, 1928.

Between 1902 and 1923, 298 infants with lead poisoning, which was chiefly caused by the white face powder used by nursing mothers, were treated in the Kyoto Imperial University Hospital. The onset of the disease usually occurred about two months after the mother began to use the powder. Of the 298 cases, 274 occurred between June 1 and October 1. The disease was found usually among the infants of merchants and laborers and seldom among the children of the agricultural class.

The mortality was 58.7 per cent. The prodromal stage averaged nineteen days and the convulsive stage, fourteen days. The commonest early symptoms were vomiting, diarrhea (green stools), bad humor, paleness, slight fever, emaciation, loss of appetite, nervousness and inactivity. Vomiting occurred among 94.3 per cent of the children; in 31.2 per cent, the vomitus resembled coffee grounds. Ninety per cent of these children died. In 68 per cent of the cases, the fontanel was tense or bulging; in 8 per cent, it was depressed.

The pupils were dilated in 8 per cent and constricted in 9 per cent; anisocoria was noticed in 6 per cent; the pupils reacted to light normally in 72 per cent, sluggishly in 24 per cent and not at all in 4 per cent. Strabismus was present in 16 per cent and nystagmus in 10 per cent. Sixty-four per cent showed some changes in the eyegrounds on ophthalmologic examination. Eleven children were blind.

In only one case was a lead line seen in the gums. The tongue was usually coated, and in several cases blisters appeared in the mouth.

The abdomen was distended in 18 per cent of the cases and sunken in 31 per cent. The liver was somewhat enlarged in most cases. In 10.7 per cent, the spleen was palpable.

Knee and ankle jerks were usually exaggerated but occasionally were weak in protracted cases. Kernig's sign was present in 31 per cent and stiffness of the neck in 35 per cent of the cases. Convulsions occurred in 73 per cent and paralysis of the limbs in only 2 per cent. The body temperature was usually between 37.5 and 38.0 C. (99.5 and 100.4 F.). The finger nails turned black in 54.8 per cent. Diarrhea was present in 83 per cent. The urine usually showed acetone, albumin, indican and urobilin. Basophilic granulation of the red blood corpuscles was found. The red blood cell count usually was diminished, and nucleated red cells were present. Relative leukocytosis and lymphopenia were found.

The spinal fluid was increased in pressure in 83.6 per cent of the cases; it was cloudy in 15.6 per cent, formed a film in 35.1 per cent and showed normal sugar concentration and increased globulin in 98.3 per cent.

HIGGINS, Boston.

Nervous Diseases

PROGRESSIVE DEGENERATIVE SUBCORTICAL ENCEPHALOPATHY. J. H. GLOBUS and I. STRAUSS, Arch. Neurol. & Psychiat. **20**:1190 (Dec.) 1928.

Personal observations in four cases and a survey of the clinical and anatomic observations in a series of twenty-two similar cases lead the authors to suggest the name of progressive degenerative subcortical encephalopathy for a demyeliniz-

ing and sclerosing process in the brain of young children; this process involves the white matter without involvement of the gray matter of the cerebral and cerebellar hemispheres. The disease may be due to some toxic factor of unknown nature which affects the normal growth of the parenchymatous structures in the subcortical regions of the brain, causes their dissolution and results in proliferative glial changes. Clinically it is characterized by a rather abrupt onset of illness, which often takes the character of a gastro-intestinal disturbance and which, after a short period of apparent recovery, is followed by a series of generalized cerebral manifestations. Among the latter, mental dilapidation, spastic paralysis accompanied by advancing rigidity, contractures and convulsive seizures appear in varying sequence. Advancing blindness with or without optic atrophy, deafness and aphasia may develop at any stage of the illness, though most frequently early in the clinical course. Some of the conditions described as chronic encephalomyelomalacia, diffuse sclerosis, sclerosing encephaloleukopathia and interlobar symmetrical sclerosis should be grouped under the general name of progressive degenerative subcortical encephalopathy.

THE BRAIN IN MONGOLIAN IDIOCY. L. M. DAVIDOFF, Arch. Neurol. & Psychiat. **20**:1229 (Dec.) 1928.

In a review of the literature and a study of ten brains from typical cases, the author is led to the conclusion that the brain in mongolian idiocy shows: (1) agenesis, as evidenced by cell poverty and failure of gyral development (there probably is also a degenerative process in early life, which increases the paucity of the ganglion cells in the cerebral cortex); (2) aplasia, as shown by its small size in comparison with that of children of corresponding age, and (3) paragensis, as demonstrated by the frequent occurrence of anomalies.

STUDIES IN STUTTERING: IV. STUDIES OF ACTION CURRENTS IN STUTTERERS. SAMUEL T. ORTON and LEE E. TRAVIS, Arch. Neurol. & Psychiat. **21**:61 (Jan.) 1929.

When the currents of muscular action from both forearms are recorded during simultaneous voluntary contractions, they may appear simultaneously in the two arms. In by far the greater number of trials, however, the action currents from one arm precede those from the other by a short interval. In records of right-handed normal speakers, the number of times that the action currents precede in the right arm far exceeds the precedence in the left, and also far exceeds the incidence of the simultaneous leads. In right-handed stutterers, the greatest number of leads is in the left arm, and the number of simultaneous leads is much greater than in the normal speakers.

AN OUTBREAK OF MENINGOCOCCIC MENINGITIS. A. CARBONELL and E. L. COOK, Mil. Surgeon **64**:49 (Jan.) 1929.

In a recent epidemic at Fort Slocum, seventeen patients with meningococcic meningitis were treated. In all cases there was a high leukocyte count on admission. The white cell count was found to be of assistance in diagnosis and treatment. The range of temperature was low in all cases; a sustained high temperature did not occur. Five patients had a rather severe petechial eruption on admission; slight albuminuria occurred in two patients; three had glycosuria on admission, and in one patient, the nasopharyngeal culture for meningococci was positive. Meningococci were found in the spinal fluid by either smear or culture in all cases. The Wassermann reaction was negative in all cases.

Nine patients had complications: There was involvement of the cranial nerves in five; of the brachial plexus in three; of the sciatic nerve in four; orchitis in one; hematuria in one, and the joints were affected in four. Nine patients, or 52.9 per cent, recovered completely. Six patients, or 31.1 per cent, became unfit for service —five on account of nerve sequelae and one on account of synovitis of the knee. Two patients died, which gave a mortality rate of 11.7 per cent.

SANFORD, Chicago.

HEIGHT, WEIGHT AND INTELLIGENCE RELATIONSHIPS IN 3,553 RETARDED SCHOOL CHILDREN. NEIL A. DAYTON, New England J. Med. **199**:934 (Nov. 8) 1928.

In 1921, a system for the psychiatric examination of retarded children in the public schools of Massachusetts became operative. The plan evolved by the late Dr. Walter E. Fernald, Dr. George M. Kline, commissioner of mental diseases and Dr. Payson Smith, commissioner of education, created a system of traveling clinics operating from fourteen hospitals and schools for mental defectives.

Of the 3,553 children examined, 72 per cent were diagnosed as feebleminded. As a group, they were of slightly less than average weight. In stature, they presented less significant variations from the standard.

An apparent relationship existed between (1) height and intelligence and (2) weight and intelligence. The groups which are over the average in height and weight comprises relatively more children of higher intelligence than the groups which are less than the average.

The mean intelligence quotient of the group that is of more than average height exceeds that of the group that is of less than average height by 7.0 ± 0.48 (standard difference).

The mean intelligence quotient of the group that is over the average in weight exceeds that of the group that is of less than average weight by 5.6 ± 0.48 (standard difference).

GENGENBACH, Denver.

FAMILY AMAUROTIC IDIOCY. P. SCOTTI, Ann. di ottal. e clin. ocul. **56**:333 (April) 1928.

The first of two cases reported was that of a girl aged 8 months, whose parents were Italians and first cousins. At 4 months of age, the infant showed irregular wandering movements of the eyes, developing into horizontal nystagmus, signs of mental and muscular degeneration and inability to sit up or hold the head up. The cranium became abnormally large. The child seemed to be well nourished. The nerves were atrophic and the characteristic white plaque with a central red spot was present in both macular regions. A bright light apparently could be seen at first; two months later, however, perception of light was abolished, and epileptiform attacks had developed. Puncture of the lateral ventricle showed high pressure of the fluid. The Wassermann reaction was negative. A brother, aged 3 years, apparently was normal.

The second patient was a girl, aged 1 year, whose parents were Jewish and not related. Nervousness and constant crying were noticed at the age of 8 months. Soon after, wandering ocular movements and general muscular weakness appeared. Ocular examination showed a condition almost identical with that seen in the first case.

The literature is carefully reviewed, with respect to the clinical picture, morbid anatomy and pathogenesis. The case described was one of the few in which races other than the Jewish were affected. The ophthalmoscopic picture is explained best as the result of a swelling and degeneration of the ganglion cells, which are most numerous in the perimacular region. The thinness of the retina in the macula explains the retention of the red color.

S. R. GIFFORD.

A CASE OF OCULAR HYSTERICAL SYNDROME. G. LODDONI, Ann. d'ocul. **165**: 357, 1928.

A patient who was struck in the left eye by a small piece of iron complained of a burning sensation of the eye, with severe pain, lacrimation and diminution of vision. After a short sojourn at the hospital blepharospasm of the left eye developed, then mydriasis, and amaurosis. Later, convergent strabismus of the right eye and nystagmus of the left eye appeared. In a few days, small conjunctival hemorrhages of three or four drops began to appear. On two occasions, about one month apart, a small piece of iron was removed from beneath the conjunctiva.

exactly where the injury had occurred. The hemorrhages occurred three or four times a day during the month, and ceased immediately when the second piece of iron was removed.

There was a suspicion of malingering, which the other symptoms more or less confirmed. Besides the blepharospasm of the left eye, the patient complained of loss of vision, followed several days later by a convulsive attack of a short duration. This attack was preceded by a severe headache and vomiting. Shortly after, a rotatory nystagmus of the right eye developed, alternating with a convergent strabismus of the left eye.

In hysteria, blepharospasm ordinarily is due to a tonic or clonic contracture of the orbicularis. When an effort was made to open the lids, the eyes would strongly converge. When the lids remained opened, the two eyes would always move in different directions. The converging spasm of the right eye became more intense the more acute the blepharospasm of the left eye became. In the left eye, a fibrillary motion existed. This motion occasionally became vertical or horizontal, then rotatory again more often than a true nystagmus. The hemorrhages resulted from the cutting of a small vessel by the pieces of iron, when the patient lay on the left side or from pressure during an attack of blepharospasm. In conclusion, the theory of hysterical autosuggestion is offered as a solution of many of the symptoms present in this case.

H. W. SCARLETT.

THE DIRECT EXCITABILITY OF THE NERVES: TETANY AND "DISJONIA." V. ZAMORANI, Riv. di clin. pediat. **26**:218, 1928.

Zamorani presents a physiologic and chemical exposition of the processes involved in tetany. The changes in the body occurring in tetany presuppose a constitutional condition. The term "disjonia" is used to designate this diathesis.

HIGGINS, Boston.

CEREBRAL ABSCESS DUE TO THE PNEUMOCOCCUS IN AN INFANT AGED TWO MONTHS. C. PELFORT and MARIA L. SALDUM, Arch. latino-am. de pediat. **22**:637, 1928.

Death occurred in an infant, aged 2 months, after an illness of fifteen days' duration. Aside from definite evidence of intracranial pressure, there were no symptoms referable to intracranial pathologic changes.

At autopsy, a large cerebral abscess occupying more than two thirds of the right cerebral hemisphere was found. The cultures revealed pneumococci as the causative factor of the abscess.

SCHLUTZ, Minneapolis.

INFLUENZAL MENINGITIS: THREE CASES. E. RULLMANN, Arch. f. Kinderh. **84**:299 (July 20) 1928.

The youngest of three patients with influenzal meningitis was 3 months old. The course of the disease was rapid, averaging about a week; all the cases were fatal. They occurred during a slight epidemic, and the symptoms of meningeal involvement, such as positive Kernig and Brudzinski signs and dermography, were seen early. The spinal fluid was turbid and gave a positive Pandy reaction.

SANFORD, Chicago.

THE PSYCHOLOGY OF CHILDHOOD. J. SUSMANN GALANT, Monatschr. f. Kinderh. **40**:407, 1928.

This article, number thirty-one of a series, deals with habit and instinct. The author quotes chiefly from Rousseau and William James in the first half of the article, and in the last half, directs a rather bitter attack on the present method of physical education of women.

GERSTLEY, Chicago.

CISTERNAL PUNCTURE IN CHILDREN. ALVIS M. MEMASHEIMER, München. med. Wchnschr. **75**:2174, 1928.

In the skin clinic of the University of Bonn, puncture of the cisterna is preferred to other methods of obtaining fluid for examination. A specially made needle, 0.8 mm. in diameter and 10 mm. long with a guide plate, is used. The method is not advised, however, for children less than 3 years of age, as ossification has not proceeded far enough to make orientation for the needle point possible.

SCHORER, Kansas City, Mo.

THE PSYCHOLOGY OF CRIPPLED CHILDREN. W. VON BAEGER, Ztschr. f. Kinderh. **34**:229, 1928.

In this monograph, the author describes the effect of crippling on the character and temperament of the child. Von Baeger believes that the psychologic reaction of the individual to his somatic make-up plays an important rôle in the construction of his character. The original cause of the crippling usually does not directly affect the character of the child if one disregards the injuries to the brain due to birth trauma, encephalitis and other factors. The first important question discussed is that of the influence of the cripple's environment on his character. In the family he may be neglected because of his helplessness and because of the expense which his care would entail, or he may become the object of too much attention and be deprived of all the benefits of discipline. Schooling is usually incomplete because of the absence of appropriate organizations in many communities. The development of the cripple's spiritual and social faculties is further hampered by his being deprived of association with his fellows. Von Baeger develops the conception of the "type ideals of childhood." He means by this term the ideal of adult manhood or womanhood which the normal child sets up as its goal. The cripple cannot, however, experience this ideal—or at most very incompletely. This arouses the question: Shall the educator develop this ideal although he knows that its realization is impossible and shall he appeal to the child's will power, pride and ambition or shall he encourage the realization of the cripple's limitations? The realization in the cripple's mind of his deformity—"Krüppelerlebnis"—is the second factor which von Baeger discusses. Some children do not recognize their condition—either because they are as yet too young, or because of a low mentality or because they have been protected from opportunities to compare themselves with other normal children. Puberty usually forces this bitter knowledge on the child; this results in the feeling of isolation, of his being different from the rest of its comrades. The child reacts in two ways: Either he withdraws himself as far as possible from contact and contrast with the world or he attempts to compensate for his condition. The individual cripple expresses these reactions in the form of an inferiority complex in envy, hate or even asocial dealings, or he compensates by an overdevelopment of normal body functions and members, by excessive vanity in personal dress and appearance, by unusual diligence and desire for personal power, by increased sexuality, etc. A characteristic sublimation of such compensation is the sincere and highly developed spirituality and piety of many cripples. The article is so well written that it deserves a careful perusal of the original. Its value is increased by the fact that the investigation was prompted by Hamburger of Heidelberg.

REICHLE, Cleveland.

SYMMETRICAL FAMILIAL LENTICULAR DEGENERATION (WILSON'S DISEASE). T. FROELICH and F. HARBITZ, Acta paediat. **8**:112 (Aug. 15) 1928.

The first child in the family died in convulsions at the age of 7 weeks. The second child was normal. The third died in convulsions at the age of 4 days; at autopsy the viscera, including the liver, were normal, but the brain showed edema and degenerative lesions in the lenticular nucleus and internal capsule. The fourth child had convulsions at the age of 2 weeks; thereafter she showed motor inactivity

and was unable to hold her head up or move the extremities normally. When seen at the age of 8 months, she showed muscular rigidity, slight stiffness of the neck, active deep reflexes, and irregular myoclonic twitchings; she died at 8 months of age in convulsions, and the autopsy showed no abnormality of the thoracic or abdominal organs. In the brain, however, degenerative lesions of the lenticular nucleus, putamen and globus pallidum were found. In spite of the age of the patients and the difference between these symptoms and the classic description of Wilson's disease, the authors believe that no other diagnosis can be made.

Calcium and Phosphorus in the Cerebrospinal Fluid in Spasmophilia. S. Ingvar, Acta peadiat. **8**:198 (Aug. 15) 1928.

The level of calcium and phosphorus was determined in the spinal fluid of nine patients with tetany and in an equal number of patients with miscellaneous clinical conditions; usually, the blood was analyzed as well. In patients with tetany the calcium in the spinal fluid averaged 4.28 mg. per hundred cubic centimeters, ranging from 3.38 to 4.89 mg., while in healthy patients its value was more than 5.14 mg. Thus, in tetany the spinal fluid calcium was shown to be diminished, but not as marked as was blood calcium. The values for phosphorus remained practically unchanged at an average level of 2.44 mg. per hundred cubic centimeters.

Tetany in a Child Aged Five Years. J. Ahlmann, Acta paediat. **8**:204 (Aug. 15) 1928.

The patient showed carpopedal spasm, laryngospasm, positive Chvostek and peroneal signs, a negative Trousseau sign, a lowered threshold of muscle irritability on galvanic stimulation, and a slightly diminished concentration of blood calcium. (The value for blood phosphorus is not given.) Although roentgenologic evidence of active rickets could not be demonstrated, the symptoms yielded rapidly to treatment with cod liver oil and a milk-free diet. No cause, either basic or precipitating, could be discovered.

Tetany and Acidosis. P. György, Acta paediat. **8**:236 (Aug. 15) 1928.

György ascribes tetany to an alkalosis. Drucker blames it on a diminution of calcium ions in the blood. This paper continues an argument that has been going on for years. No new facts are offered.

McIntosh, Baltimore.

Pharmacotherapeusis of Epilepsy. Vladimir Vondraček, Čas. lék. česk. **65**:24 (Jan.) 1926.

The advantage of protein therapy in epilepsy is the simplification and enhancement of the medication as phenylethylbarbituric acid, potassium tartaricoboraxate and bromide salts. The foreign proteins used included a mixture of milk and vaccines. The author's summary is as follows: The frequency and intensity of the convulsions do not have any bearing on the subsequent result of treatment, though usually petit mal is more amenable to treatment than grand mal. Treatment must be carried on for years. Dosage should be kept as low as results will warrant. The patient must be under supervision. Protein therapy is not a cure for epilepsy, but smaller dosage of essential medication is made more potent. Each epileptic patient should have at least one thorough neurologic examination to rule out symptomatic epilepsy and to outline a proper program of management.

Infratemporal Drainage in Congenital Internal Hydrocephalus. Vana Antonin, Čas. lék. česk. **65**:20 (Jan.) 1926.

The author reviews the theories of the production of hydrocephalus and gives a historical résumé of the various operations used in treatment. This includes such radical measures as nephrectomy and transplanting of the free ureter into the spinal canal. The infratemporal method of drainage has all the advantages

of the method of Hildebrand, including gravity drainage, and in addition obviates the orbital edema and irritation by ultimate drainage along the tissues of the face and neck into the mediastinal tissues. The sphenoidal portion of the temporal bone is trephined just above the pons of the zygoma.

STULIK, Chicago.

PURULENT MENINGITIS IN INFANTS. A. M. DESCHTYZ, Pediatria **12**:196, 1928.

The author discusses the frequency with which purulent meningitis occurs in infants and the difficulties connected with diagnosis. Many cases are often diagnosed only post mortem. During 1926 and 1927, the author studied 246 cases of meningitis, of which 67 were of the purulent type. Of these 67 cases, 50 per cent occurred in infants up to 1 year of age.

Outside of cerebrospinal meningitis, purulent meningitis is often seen as a complication of pneumonia, erysipelas, infections of the upper respiratory tract, pyodermia and other septic infections. Infants, however, often fail to show any localizing symptoms; disturbances of speech, an extremely important sign in the adult, cannot, of course, be ascertained. The increase in intracranial pressure may at first be masked somewhat by the gradual separation of the sutures of the skull.

According to the author, the majority of cases of purulent meningitis lead sooner or later to a block somewhere in the path of the cerebrospinal fluid, usually in either the foramen of Magendie or the foramen of Luschka, the cisterna cerebromedullaris, or the spinal canal.

The bulging of the fontanel, which is not relieved by a spinal puncture, is one of the most important signs of the existence of a block. The different character of the spinal fluid obtained by spinal, cisternal or ventricular punctures is another important evidence of the existence of a block:

The author's conclusions are as follows:

1. Purulent meningitis in infants often leads to the formation of a block somewhere in the path of the spinal fluid.

2. The characteristic observations in these cases are: the small amount or absence of fluid following spinal punctures; the persistent bulging of the anterior fontanel following a spinal puncture; the different character of the fluid obtained by spinal, cisternal or ventricular punctures, and the frequent xanthochromia of the fluid.

3. Blindness often follows these attacks of meningitis.

4. In these cases of "blocked" meningitis, recovery does not often occur.

CONTENT OF THE SUGAR AND KETONE BODIES IN THE SPINAL FLUID AND IN THE BLOOD IN VARIOUS FORMS OF MENINGITIS AND DISEASES OF THE CENTRAL NERVOUS SYSTEM. E. A. GORNITZSKY, Pediatria **12**:204, 1928.

The author has studied carefully the sugar and the ketone bodies in the blood and spinal fluid of normal persons and in thirty-five patients with various diseases of the central nervous systems. His conclusions are:

1. The sugar content of the spinal fluid in normal patients is about 20 or 30 mg. per hundred cubic centimeters less than that of the blood.

2. The sugar content of the spinal fluid in the various forms of meningitis begins to decrease in the early stage of the disease.

3. The subsequent curves of the sugar content differ in the different kinds of meningitis. (*a*) In tuberculous meningitis, there is a constant fall in the sugar content of the spinal fluid, reaching at times to the low level of 10 mg. per hundred cubic centimeters. (*b*) In serous meningitis, the sugar of the spinal fluid gradually increases. (*c*) In cerebrospinal meningitis, also, the sugar content rises, but a fall may take place in the later stages of the disease.

4. The sugar content of the spinal fluid is increased in cases of meningitis following scarlet fever.

5. The sugar content is also increased in cases of epidemic encephalitis, syringomyelia and chronic hydrocephalus.

6. In cases of poliomyelitis, epilepsy and chorea, the sugar content of the spinal fluid is within normal limits.

7. The blood sugar is increased in tuberculous meningitis; in the other forms of meningitis, it is within normal limits.

8. In tuberculous meningitis the blood sugar is between 90 and 120 mg. per hundred cubic centimeters higher than that of the spinal fluid. In serous and cerebrospinal meningitis, the difference is only from 40 to 50 mg. per hundred cubic centimeters.

9. The spinal fluid should be examined in from three to four hours after the spinal puncture; a longer interval materially affects the results. The blood should be withdrawn before the spinal fluid.

10. The study of the sugar content of the blood and of the spinal fluid may be of great diagnostic value.

11. The study of the ketone bodies of the blood and of the spinal fluid does not have a diagnostic value.

GASUL, Chicago.

CLINICAL OBSERVATION OF ACETORACHIA. TAKASHI WAKAGI, J. Pediat. (Tokyo) Sept. 20, 1928, no. 340, p. 1485.

The presence of acetone in the cerebrospinal fluid has been known chiefly in diabetic coma; it appears also in the last stage of Addison's disease, in syphilitic encephalitis, in epilepsy, in burn, in cerebral hemorrhage, in tuberculous meningitis, in lead palsy and in chronic alcoholism. The acetone in the cerebrospinal fluid seems to be a secondary migration of acetone in the blood, but it may cause a partial coagulation of globulin resulting in the increased turbidity of the fluid. It must be remembered also that as acetone has a slightly hemolytic effect, its presence in the fluid may cause erythrochromia or xanthochromia.

KATO, Los Angeles.

SEROUS MENINGITIS CAUSED BY INFANTILE LEAD POISONING BEFORE AND AFTER THE DISCOVERY OF THE CAUSE BY PROF. I. HIRAI. T. IZUKA, Orient. J. Dis. Inf. **3**:42, 1928.

The cause of the infantile serous meningitis prevalent in Japan was found by Professor Hirai in 1923 to be due to lead in the white face powder used by the nursing mothers. For the previous two years, the mortality was 66 per cent and for the subsequent two years, 37 per cent. The incidence of the condition, especially among the well-to-do classes and in the environment of the university, has diminished.

HIGGINS, Boston.

Diseases of the Ear, Nose and Throat

A PHYSIOLOGICAL THEORY OF READING DISABILITY AND STUTTERING IN CHILDREN. SAMUEL T. ORTON, New England J. Med. **199**:1046 (Nov. 22) 1928.

In 1925, the author published a preliminary report of a study of a group of children who were retarded in reading and who seemed to him to show a complex of symptoms which differentiated them from normal readers. At one extreme of this group was a case of such severity that it would be universally characterized as congenital word blindness, while the remainder of the children seemed to form a graded series extending from that to the normal condition. In the past there has been a tendency to regard the more severe cases as pathologic in nature and the less marked ones as merely cases of slow acquisition of reading. The only criterion, however, by which these two groups could be separated was the opinion

of the examiner. In the report it was pointed out that there were certain errors which seemed to characterize the attempts of these children to read and which suggested a physiologic rather than a pathologic basis. A tentative explanation was offered on the basis of confusion in cerebral dominance (*Arch. Neurol. & Psychiat.* **14**:581 [Nov.] 1925).

In further investigation of the condition, the author conducted at the Iowa State Psychopathic Hospital "a study of 175 children who showed a selective retardation in reading below both mental age and school grade placement. By this method of selection there was obtained a group of retarded readers without regard to the character of their reading performance, and to these children was given an examination designed to discover the frequency of certain types of errors in their attempts at reading. As a control series, the same examination was given to 120 children who were reading with the facility expected for their mental age and grade placement. The results of this work are soon to be published in detail but I may anticipate their appearance by the statement that these studies bear out strikingly my earlier contention that reading disability forms a fairly clear-cut clinical entity which can be diagnosed by the frequence of certain types of errors and that our series of tests will also serve to grade cases according to the severity of their handicap."

Experimental studies were also conducted in the field of stuttering. The act of stuttering was found to be characterized by a striking failure of the orderly integration of the various reflex groups which coordinate in the production of speech. "Thus we have records in which the direction of motion of the chest and abdomen are synchronously opposed, the chest inhaling while the abdomen exhales and vice versa, thus counteracting each other, so that no breath stream is passing the larynx. Again, the larynx, which normally makes many up and down excursions in vocalization independently of the expiratory movements, is seen in some of our records to move in time with the abdomen or with the chest. We have also found evidence of both tonic and clonic spasms in the muscles of the vocal mechanism during stuttering. The tonic spasms show themselves in both the kymographic records of the movements of the chest, abdomen and larynx and also in the fixed tones which can be shown by plotting photographic records of the speech vibration. The clonic spasms are perhaps best shown by the occurrence of a vibrato in the stutterer's speech. The vibrato is a rapid fluctuation within a narrow range of pitch which is found in singing, in intoning and probably also in strongly emotional colored speech but is not found in normal fluent propositional speech."

In conclusion the author says: "Whether or not the theoretical outline for the two conditions of reading disability and stuttering here presented will stand the test of further study and more intimate knowledge of brain function and brain structure, we can at least say that this physiologic concept offers a much more hopeful prognosis than that of the agenetic focal brain condition which has been its chief precursor as a theory of the etiology of wordblindness or than the most intangible emotional variant which has held sway in stuttering. Our new envisagement also has suggested some distinctive lines of experimental attack on retraining which we have already found highly effective in overcoming the reading impediment and promising in stuttering."

GENGENBACH, Denver.

THE TREATMENT OF OTORRHEA. J. A. KEEN, Practitioner **121**:35 (July) 1928.

At the present time the most widely discussed operative treatment for disease of the middle ear is zinc ionization. In the present series, one half of the patients were treated by ionization.

Methods of treatment without ionization are discussed.

The author's favorite method consists of insufflations of boracic powder. The meatus and canal are cleaned out with cotton applicators and the canal then filled with boracic powder by means of a powder blower. No treatment at home is ordered except to keep the ear dry.

When the patient does not seem to make progress with the insufflations of boracic powder, bismuth and iodoform powder are used. The fear held by many otologists that this method is dangerous is groundless.

The underlying principle is to seal off the middle ear as far as possible from reinfection; syringing, even by the surgeon himself, must be considered harmful.

Ionization as an additional measure was done in the other group.

The author concludes that both methods are equally efficient, but that the ionization method is much more rapid. In addition, in recent years he has practically abandoned the so-called conservative mastoid operation, as he feels that persevering with the operative measures in use at the present time would have succeeded just as well.

GELSTON, San Francisco.

Diseases of the Skin

THALLIUM ACETATE IN RINGWORM OF THE SCALP. BERNARD APPEL, New England J. Med. **199**:733 (Oct. 11) 1928.

The author refers to the frequent failures of the usual fungicide treatment. He mentions the efficacy of roentgen treatment but points out the increasing recognition of the danger that it may result in partial or total permanent alopecia. He refers to the article of Felden (*Arch. Dermat. & Syph.* **17**:182 [Feb.] 1928) on a series of forty-seven cases of ringworm of the scalp in which epilation was effected by thallium acetate, and includes the results in seven cases of his own. Eight and five-tenths milligrams per kilogram of body weight was given by mouth in a half glass of sweetened water. Hair usually began to come out in from nine to fourteen days and was totally out in three weeks. It began to grow in again in from two to four weeks. An interesting observation was that in all these cases the eyebrows, the lashes and a thin line along the frontal edge of the scalp were not affected. As a local treatment, the author used an ointment consisting of 0.05 drachm (30 grains) of salicylic acid, 1 drachm (60 grains) of precipitated sulphur and petrolatum or boric ointment. This was rubbed into the scalp thoroughly, morning and evening. The author concludes that the administration of thallium acetate in the proper dose, to selected children before the age of puberty, is the best method of epilation in cases of ringworm of the scalp.

IMPETIGO NEONATORUM: ITS CONTROL AND TREATMENT. ORVILLE R. CHADWELL, New England J. Med. **199**:983 (Nov. 15) 1928.

Impetigo neonatorum is a communicable skin infection of new-born infants. It is seen most frequently in lying-in institutions.

The author believes that the invading organism is usually one of the staphylococcic group, whether the condition is impetigo neonatorum, impetigo contagiosa or pemphigus neonatorum; and that the age of the child and the virulence of the particular strain are responsible for the variations in the appearance and course of the disease. In the new-born infant, the impetigo does not often become crustaceous as in the older child; rarely is the disease virulent enough to justify the erroneous term pemphigus.

The author has been seeing between 1,500 and 2,000 new-born infants annually for a period of several years. His observations differ somewhat from descriptions of the malady found in certain textbooks.

The disease is commonly sporadic, but if it becomes epidemic in a large institution it is more likely to do so in the hot, humid months when nurseries are commonly overheated. Then the most frequent site of the lesions is in the axillae and the groins, due possibly to maceration of the skin from sweating and ensuing easier inoculation.

The typical lesion is likely to be observed first as a bulla or bleb. In the beginning, it shows a clear serous content. Later, a white or yellow purulent content appears which varies according to the type of staphylococcus present. There is a slight areola of redness. In the majority of cases the lesion appears to be discrete, and there is an entire absence of systemic signs.

In sporadic cases, infected areas on the face and head are seen occasionally. These are usually produced by the finger-nails of the infant. The lesions present more of the characteristics of the disease as it occurs in older children, particularly as to the formation of crusts.

For the control of the condition, the author uses the following methods:

Prophylaxis.—As soon as the eyes are cared for in the delivery room and the routine dose of adult blood is administered, the infant is sent to the floor nursery. Here it receives its only washing with soap and water during the sojourn in the institution. Following the removal of vernix and blood by this washing, the infant is "larded" thoroughly with 5 per cent ointment of ammoniated mercury. The orders are given to rub the ointment in, not on the skin. All subsequent care of the skin consists of a daily thorough inunction with sterile cottonseed oil. In theory, this practice aids in impregnating the pores of the skin still more with the mercurial ointment. When diapers are changed, the invariable rule is to wipe off the parts with absorbent cotton and sterile oil, without water. In so large an institution, the advantages of this omission of bathing with water are numerous.

Isolation.—The smallest skin lesion is reported immediately to the resident or visiting pediatrician by the nurse. This report usually is not made until the infant has been put "on precautions" as a routine. This hospital has a small, so-called isolation room, for each nursery, and the physicians of course depend on frocking and the prevention of finger contacts. Every case of pyodermia, however simple, is regarded as a potential case of impetigo and is subjected to the following routine, in private or house patient:

Treatment.—Any suspicious lesion is evacuated and the area thoroughly anointed with a 5 per cent ammoniated mercury ointment twice daily. Practically speaking, this is the end of the episode. If new lesions do not appear in three days, the infant is returned to the nursery. If several typical lesions are present on an infant, not only is the foregoing technic carried out, but in addition the entire surface of the skin of the infant is thoroughly rubbed daily with a 3 per cent ointment of ammoniated mercury.

GENGENBACH, Denver.

ACRODYNIA. R. TURQUETY, Nourrisson **16**:297 (Sept.) 1928.

The term acrodynia was coined in 1828 by Chardon in describing an epidemic of a new disease which ravaged Paris at that time and affected 40,000 persons. The epidemic quickly died out, and no further mention is found in the medical literature until 1903, when Selter of Solingen described a similar syndrome; then followed the reports from Australia, beginning in 1914. These have been followed by reports from many other countries. In the Paris epidemic, only adults were attacked; the recent epidemics of acrodynia claim only the children. This in itself would seem to be sufficient to deny the identity of the two conditions though the symptoms and evolution are quite similar.

In depicting the clinical picture, the author, in addition to the striking cutaneous lesions, emphasizes the symptoms connoting a widespread involvement of the vegetative nervous system: asthenia, profuse sweating, sialorrhea, increased lacrimation, constipation, alternating cyanosis and erythema and psychotic alterations. He feels that a preponderance of evidence favors an infectious etiology with the portal of entry in the nasopharynx. The symptom-complex and course of the disease suggest extensive involvement of the mesencephalon, thus raising the question of a possible relationship between acrodynia and epidemic encephalitis.

Under treatment, the beneficent effects of ultraviolet ray therapy are extolled.

McCLELLAND, Cleveland.

INSULIN THERAPY IN DESQUAMATIVE ERYTHRODERMIA OF NURSING INFANTS WITH MARKED ATROPHY. CATERINA DESSYLLA, Riv. di clin. pediat. **26**:583, 1928.

"Érythrodermie désquamative," a manifestation of an exudative diathesis, was first classified as an entity by Moussous-Leiner. It appears when the child is quite young, and not only skin lesions, but also a profound disturbance of the metabolism and growth appear. Various causes for the condition have been suggested, such as autointoxication, anaphylaxis, lack of vitamins and endocrine disturbance. One rather constant symptom noted by the author was a high percentage of blood sugar during fasting; the more severe the condition is, the greater is the amount of blood sugar, as shown in the following table:

Number Cases	Severity	Blood Sugar, PerCent
2	Mild	0.93
4	Moderate	1.20
3	Severe	1.33
3	Extremely severe	1.54

Insulin treatment, therefore, seemed advisable. The dose of insulin given to the infants was at first from ½ to 1 unit, and was increased to 3 or 4 units daily.

Eight breast-fed infants, varying in age from 1½ to 5 months, are discussed. The author considered that treatment with insulin caused improvement in six of the eight cases (75 per cent). The usual result from other methods of treatment in such cases is improvement in 50 per cent of the cases.

HIGGINS, Boston.

THERAPEUTIC PROCEDURE IN ALLERGIC ALIMENTARY URTICARIA OF CHILDREN. A. ARGÜELLES TERÁN, Arch. españ. de pediat. **12**:303, 1928.

Following experiments of J. Mayr and Moncorp, who found that the administration of splenic extract could modify eosinophilia, pruritus and allergic asthma, the authors used extracts of this sort in intractable urticarias of alimentary origin. The results were favorable in a number of cases.

The splenic extract is given before meals in a teaspoonful of water, slightly acidulated with dilute phosphoric or hydrochloric acid. The action is believed to be in the nature of a deamination process initiated by a splenic hormone.

ERYTHEMA NODOSUM IN AN INFANT AGED NINETEEN MONTHS. VICTOR RAGGIO, Arch. latino-am. de pediat. **17**:599, 1928.

Erythema nodosum rarely occurs in an infant of this age.

Tuberculous lesions were present in the lungs. The Pirquet reaction was intensely positive.

The disease is not infrequent among children more than 5 years of age. In practically all his cases, the author observed positive tuberculin reactions. This fact rather supports the theory that manifest or latent tuberculosis is associated in some manner with the manifestation of the condition.

SCHLUTZ, Minneapolis.

REVIEW OF DERMATOLOGICAL LITERATURE IN PEDIATRICS FOR 1927. CARL LEINER, Monatschr. f. Kinderh. **40**:385, 1928.

A thorough review of the literature is presented in a manner consistent with the great reputation of the author. One or two points are of special interest.

The question of the inheritability of congenital syphilis is still undecided. Erich Muller recommends a new treatment for congenital syphilis: twelve intravenous injections of neoarsphenamine and twelve intramuscular injections of mild mercurous chloride in the course of twelve weeks. He uses 0.04 neoarsphenamine instead of 0.03, and 2 mg. of mild mercurous chloride instead of 1 mg. per kilogram of body weight. Some observers have returned to the oral administration of acetarsone, a preparation containing 27 per cent of arsenic. Von den Steinen begins with a fourth of a tablet and increases rapidly to a whole tablet.

In scarlet fever, it is generally agreed that the cause of the disease is the hemolytic streptococcus. One or two authors question the absolute specificity of the scarlet fever streptococcus.

Degkwitz claims that he can procure the measles virus from the blood, pass it through a Berkefeld filter and continue it through from sixteen to eighteen generations. In chickenpox, Knöpfelmacher has shown that subcutaneous injections of 1 cc. of the virulent lymph in a dilution of from 1:100 to 1:200 will immunize children for a year.

In erythema nodosum, Landau does not admit the common etiology with rheumatism.

Nothing new is offered in the treatment for eczema.

TWINS WITH LYMPHANGIECTATIC EDEMA. HELENE MASLOWSKY, Monatschr. f. Kinderh. **40**:436, 1928.

Nothing is known as to the etiology of this condition, described in a case report. In this case, the mother suffered from a nephritis of pregnancy.

GERSTLEY, Chicago.

ERYTHEMA NODOSUM: A COMPARISON BETWEEN A ROENTGENOGRAM OF THE LUNG AND THE SEVERITY OF CLINICAL SYMPTOMS. U. CARLBORG, Acta paediat. **8**:210 (Aug. 15) 1928.

In the years from 1923 to 1926, 110 patients with erythema nodosum were admitted to the Gotenburg Children's Hospital. Of these, 79 were studied by x-rays. Of the children showing the disease prior to school age, the numbers with marked, and the number with mild, changes of the hilum were approximately equal; in the children of school age, on the other hand, marked involvement of the hilum was rarely found. No relationship could be demonstrated between the extent or severity of the eruption and the pulmonary lesions. A persistent high fever occurred more frequently in patients with extensive shadows of the hilum.

MCINTOSH, Baltimore.

Surgery and Orthopedics

THE AFFECTIONS OF THE APPENDIX IN YOUNG CHILDREN; A REVIEW OF ONE HUNDRED CASES. E. W. PETERSON, Ann. Surg. **89**:48 (Jan.) 1929.

Peterson brings out the fact that appendicitis in early life is by no means as uncommon as the texts would imply. A diagnosis is made with great difficulty, particularly in the case of the children, due to the fact that the permanent position of the appendix has not been attained, and that it usually lies rather above than below McBurney's point. It may be found, however, almost anywhere in the abdomen or pelvis, under the liver, or even on the left side of the body. Mortality in acute appendicitis in early life is high, being over 70 per cent in nurslings, and from 15 to 40 per cent in children less than 6 years of age. Purgation, and the procrastination of the surgeon are weighty factors in this high mortality. The review of the author's 100 cases brings out the relationship between intussusception and disease of the appendix, and the frequent relationship between a pathologic condition of the appendix and hernia. Of the 100 cases, 25 were of the type described as "chronic," being reported pathologically as chronic, healed or healed purulent appendicitis. Characteristically these patients given a history of recurrent attacks of abdominal pain of short duration, with nausea and slight fever, and either with or without emesis.

OBSTRUCTIVE HYDRO-URETERAL ANGULARITY WITH HYDRONEPHROSIS IN CHILDREN. FRANK HINMAN, Arch. Surg. **18**:21 (Jan.) 1929.

This extensive paper, dealing with various causes of obstruction to the urinary passages in children, does not lend itself easily to fair abstraction because of the great wealth of information it contains.

The following is an excellent analysis of cases of obstructive hydro-ureteral angularity and summary of surgical treatment. First Stage: A nephrostomy is performed on both sides or on the more diseased side; the upper ureters are straightened and freed and are then splinted with the nephrostomy tubes. Second Stage: The bladder and lower ureters are exposed through a midline suprapubic incision. Each ureter is straightened and freed either to its pelvis or, when nephrostomy has been done, to the free portion above. Enough of the lower portions are resected to take up the slack and, after the bladder is opened, they are implanted in the opening into the bladder made by resection of the old ureterovesical orifice. Large catheters are inserted into the ureters for a considerable distance as splints and for drainage and lavage. The vesical neck is thoroughly inspected, and any bar or contracture that is present is resected. The bladder is closed around a suprapubic drainage tube and the ureteral catheters.

INTESTINAL OBSTRUCTION IN INFANTS: REPORT OF TWO CASES. ALEXANDER SOGLE, M. J. & Rec. **128**:343 (Oct. 3) 1928.

Case 1 was in an infant, aged 13 months. The obstruction was caused by an intussusception. Case 2 was in an infant, aged 3 months. The obstruction was caused by a strangulated inguinal hernia. Both patients were operated on a few hours after the onset of symptoms, and both made an uneventful recovery.

WILLIAMSON, New Orleans.

EXTRA-ARTICULAR IMMOBILIZATION OF THE HIP JOINT. H. C. SCHUMM, Surg. Gynec. Obst. **48**:112 (Jan.) 1929.

An operation devised to bring about immobilization of the hip joint in cases of tuberculosis and osteoarthritis is described. The advantage of the method

is the absence of disturbance and the dissemination of an infectious process by keeping the operation outside of the joint. The operation has given satisfactory results in nine cases, the details of two cases in children being cited. After a longitudinal incision is made over the trochanter, and up on the ilium, a chisel is used to make a shelflike cut into the side of the ilium; into this cut is inserted the upper end of the graft, which is taken from the femur. The femur is used because it is stronger than the tibia, and its use avoids multiple incisions. The chisel is then used to turn away from the trochanter an anterior and posterior flap; the lower end of the graft is inserted into the groove between the flaps. The union has been uniformly satisfactory, and the operation is recommended for patients with tuberculosis and osteoarthritis.

GEORGE H. JACKSON, Chicago.

A CASE OF DIAPHRAGMATIC HERNIA IN AN INFANT. GLADYS H. DODDS and J. D. S. FLEW, J. Obst. & Gynec. Brit. Emp. **35**:737, 1928.

The only case of diaphragmatic hernia seen in 800 infants born consecutively and in 200 autopsies on infants is described. In a majority of the cases, the abdominal organs simply pass through an opening in the diaphragm, not constituting a true hernia but a spurious diaphragmatic hernia. The true diaphragmatic hernia projects into the pleural cavity through a space in the muscle covered by peritoneum and pleura. Among 80 case reports of congenital hernia collected by Bohn, a hernial sac was present in only 14. The left side is more frequently affected than the right. Of 42 diaphragmatic hernias, according to Popp, thirty-seven were on the left side and only five on the right. According to Ballantyne, the male sex seems to be more liable to diaphragmatic hernia than the female; thus, in 67 patients examined by him, there were 47 males and 20 females.

The case is reported in detail with the history, physical observations and postmortem data. Postmortem examination showed a combination of unusual features: (1) a spurious diaphragmatic hernia; (2) abnormal fissuring of the liver; (3) a mesentery attached to the gallbladder; (4) an early embryonic type of peritoneal relation to the abdominal viscera, and (5) a carcinoid tumor.

ADAIR.

BILATERAL PSEUDOCOXALGIA. CECIL P. G. WAKELEY, Proc. Roy. Soc. Med. **22**:5 (Nov.) 1928.

The patient, aged 4 years, had walked badly since the age of 2. He had been treated for rickets in various hospitals. The author was consulted during September, 1928, because of the child's waddling gait. Examination disclosed that all movements at the hip joint were free except abduction, which was limited bilaterally. Clinically, there was no evidence of rickets. Roentgen examination showed healed rickets and revealed a condition of bilateral pseudocoxalgia at the hip joint. The upper femoral epiphyses were flattened and poorly developed.

WILLIAMSON, New Orleans.

INTUSSUSCEPTION IN CHILDREN. E. EDBERG, Acta paediat. **8**:130 (Aug. 15) 1928.

The author observed sixty-seven patients with intussusception, ranging in age from 1 month to 12 years. About two thirds of the cases occurred during the first year of life. Twice as many boys as girls were affected. In the author's opinion, intussusception usually starts as the invagination of a localized thickening in the intestinal wall — in the majority of cases, a thickened Peyer's patch. Four of the cases appeared to be caused by Meckel's diverticula associated with this

condition. Surgical treatment is indicated from the outset. The mortality was 36 per cent for the entire series of cases, which included many patients whose condition was hopeless by the time they were brought to the hospital.

McINTOSH, Baltimore.

Miscellaneous

RADIUM NECROSIS OF BONE. D. B. PHEMISTER, Am. J. Roentgenol. **16**:340 (Oct.) 1926.

Uninfected necrotic bone produced by radium implantation, when subsequently used for weight bearing, will be slowly replaced by ingrowing new bone by creeping substitution. When the necrotic bone is not used, as a result of nonunion of fracture through it, the necrotic bone will be sequestrated from the living bone and slowly absorbed. Because of the radium burn of the adjacent tissues, the rate of creeping substitution by new bone or of absorption is much slower than in the case of aseptic necrotic bone, the result of circulatory disturbance or the application of chemicals. Secondarily infected areas of bone killed by radium undergo sequestration, whether or not they function mechanically. Uninfected, radium-killed bone is gradually replaced by new bone when it functions in the support of a part during the treatment of tumors. When a small necrotic portion borders on an articular surface, it does not become detached and go free into the joint as a joint mouse.

RIGHT-OBLIQUE-PRONE POSTURE FOR STUDY OF THE ESOPHAGUS. WILLIS F. MANGES, Am. J. Roentgenol. **16**:374 (Oct.) 1926.

The right-oblique-prone position is especially useful in studying lesions of the lower three fourths of the esophagus. The erect position, however, is best for lesions of the upper portions. The advantage of this position is that the parts of the esophagus both distal and proximal to the stricture or lesion are distended with a mixture of barium sulphate. Moreover, the lower end is at a higher level than the upper end, and the force of gravity aids materially in keeping the distal portion of the esophagus distended.

STULIK, Chicago.

THE SIGNIFICANCE OF LYMPHOCYTOSIS IN INFANTS AND CHILDREN. ISAAC A. ABT and JOHANNA HEUMANN, M. Clin. N. Amer. **12**:21 (July) 1928.

During childhood the lymphatic apparatus is much more developed than in adult life and responds more intensively to disease, irritants and infectious processes. The function of the lymphocyte is varied. It is capable of phagocytosis; it may assist in the digestion of fat, may become a fibroblast, may act as a neutralizing agent against certain alimentary toxins and may perform an important part in the defense of the body against bacterial disease. The presence of lymphocytosis is interpreted by some hematologists as an indication of an active defensive mechanism. It occurs in childhood in those infections which in the adult would disclose a polymorphonuclear leukocytosis. An increase in the number of lymphocytes in the blood occurs after physical exertion, during whooping cough and German measles, in glandular fever and mononucleosis, in tuberculosis before extensive destruction of the lymph nodes has taken place and commonly during recovery from various acute infective processes. The cause and significance of lymphocytosis, however, have not been established satisfactorily. This is especially true of the relationship between the increase in lymphocytes and the glands of internal secretion. In view

of the variations which may occur in both health and in disease, all possible causes of a high lymphocyte count should be considered in differentiating a benign increase from grave and fatal disorders of the blood.

SMITH, OGDEN, UTAH.

THE DEVELOPMENT OF CHILDREN BORN OF PREVIOUSLY IRRADIATED MOTHERS. WALTHER SCHMITT, Monatschr. f. Geburtsh. u. Gynäk. **80**:157 (Oct.) 1928.

The general impression has been that the children of mothers who received roentgen therapy preceding their pregnancy did not develop normally. Schmitt observed forty-two mothers who had received therapeutic irradiation before, and in some cases probably during their pregnancy. Eight mothers aborted, two were delivered prematurely and thirty-one at full term; twenty-eight of the thirty-four new-born infants were normal physically, four were poorly developed and two were premature. One congenital heart lesion was found. During the first year, five children died. The remaining children were examined frequently. Four were from 2 to 7 pounds (907 to 3,175 Gm.) underweight according to the standards of Pirquet and Camerer. All were normal mentally. In one boy, aged 6½ years, with a normal amount of blood sugar, a reducing substance was found in the urine. A test for fermentation gave negative results. Another child, aged 3½ years, had persistent shaking of the head.

The results show that roentgen treatment is not always followed by injury to the offspring. The author urges similar observations in other clinics.

BRAHDY, New York.

PHENYLETHYLHYDANTOIN SICKNESS, WALTER LESIGANG, Monatschr. f. Kinderh. **40**:289, 1928.

Of 106 children treated with phenylethylhydantoin — a drug similar to phenobarbital, thirty developed fever and exanthem. In the majority, the rash appeared from the seventh to the twelfth day. In only one patient did the exanthem appear immediately after the first dose. On the other hand, in eleven of twelve cases one dose of phenylethylhydantoin brought on the fever and exanthem when given from the eighteenth to the thirty-ninth day. These facts led the author to conclude that the sickness caused by the phenylethylhydantoin was not due to a toxic effect of the drug but to an allergic phenomenon. Intracutaneous reactions are marked whether the drug has been given before or not. Blood transfusions performed while the patient is sick do not produce hypersensitiveness. Phenylethylhydantoin is of value in chorea and epilepsy, but is of little use in pertussis.

GERSTLEY, Chicago.

A COCAINE REACTION IN A CASE OF INTOXICATION. J. MARTINHO DA ROCHA, Arch. Pediat. **1**:37 (Nov.) 1928.

An infant, aged 4 months, with diarrhea, vomiting, fever and other signs of an extreme intoxication, was given 0.04 Gm. of cocaine hydrochloride in a 60 cc. solution of sodium citrate. The child soon showed dilatation of the pupils and dry mucous membranes. The following day there was an elevation in temperature, cyanosis of the face and extremities, and tremors and disorganized movements of the entire body. Dextrose was given intraperitoneally, and the child recovered. From a review of many similar cases in the literature, the author concludes that cocaine is contraindicated in early infancy in digestive disturbances, grip, pyelitis and other infectious diseases.

SANFORD, Chicago.

THE DOSAGE OF MEDICINE IN CHILDREN. GERTRUDE FUCHS, Ztschr. f. Kinderh. **46**:280 (July) 1928.

The usual dosages of medicine, based on empiricism, employed for adults and children are compared, with good agreement, with a dosage calculated from the square of the sitting height. The conclusion is drawn that for most medicines a dosage based on the square of the sitting height is permissible. A table gives the dosage for the sitting height from 35 to 85 cm.

EMERSON, Boston.

THE RELATION BETWEEN THE SIZE OF THE FAMILY AND THE QUALITY OF THE CHILD'S SCHOOL WORK. A. BUSEMANN, Ztschr. f. Kinderforschung **34**:553, 1928.

The author gives additional statistics which substantiate the conclusions of his previous publication (abstr., THE AMERICAN JOURNAL OF DISEASES OF CHILDREN **36**:855 [Oct.] 1928). The poorest work was done by children who had no or one brother or sister and by those who had five or more. The only boy or the only girl did poorer work than the others. The oldest child of the family did better work than the youngest. These conclusions do not hold true for families of low economic standard.

REICHLE, Cleveland.

ORTHOPEDIC CONDITIONS ESPECIALLY RELATED TO PEDIATRICS. K. TAKAGI, J. Pediat. (Tokyo), Dec. 20, 1928, no. 343, p. 2181.

Takagi calls the special attention of pediatricians to the following orthopedic conditions: (1) congenital dislocation of the hip joint; (2) dislocation of the hip joint following osteomyelitis in infants; (3) tuberculous arthritis of the hip joint; (4) Perthes' or Calvé's disease, usually seen in children between 5 and 15 years of age; (5) Heine-Medin's disease; (6) Rust's disease, and (7) laterotorsio cruris (Takagi).

KATO, Los Angeles.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Clinical Meeting, Children's Memorial Hospital, Nov. 20, 1928

JOSEPH BRENNEMANN, M.D., *Chief of Staff, Presiding*

CONGENITAL ALOPECIA. DR. ROBERT BLESSING.

The patient, a girl, was first seen in the clinic four years before presentation and gave the history that since birth there had been a total absence of hair on the scalp, with the exception of a few black scalp hairs at birth. At the age of 6 weeks she was completely bald. There was no history of alopecia in the family for two generations. She was first seen in the clinic for patients with syphilis a year and a half before presentation, and was discharged as normal clinically and seriologically. She was seen at the clinic from July, 1927, to July, 1928, and was given thyroid medication with no improvement. She ceased attendance at that time, to return a few days before presentation. Dr. E. A. Oliver presented her to the Chicago Dermatological Society as having a case of congenital alopecia. She had a few hairs on the eyebrows and a few eyelashes, which could easily be counted.

This disorder has been described chiefly by dermatologists, and there is little mention of it in pediatric literature. It is attributed to a defect of the ectoderm, with either absent or poorly developed hair follicles. The prognosis depends on the condition of the hair follicles. It is rather difficult to differentiate the condition from total alopecia areata, but that disorder usually appears after the fifth year.

The patient has been given some ultraviolet irradiation since her return to the clinic.

ALLERGY (SILK SENSITIZATION). DR. M. S. FINK.

The patient, a girl, was seen about a month before presentation, with a few vesicular patches about the chest and arms, accompanied by itching. She gave a history of having had infantile eczema from the age of 2 months. The mother said that the child could not come in contact with silk without developing irritation. The arm was stimulated with silk; a silk necktie was tied about one arm, and the other was wrapped in a cotton bandage as a control. The test was repeated on the evening of presentation, and it was seen that there was an immediate, intense reaction in the form of a large wheal, or a group of closely related wheals, in addition to edema. The opposite arm appeared perfectly normal.

Some work has been done in connection with this sensitization, which attempted to prove that it was due to a glue which originated in the mouth of the silkworm, but it was shown that the glue was all washed out in the manufacture of silk, leaving only a protein which was readily reduced to one of the amino-acids. The only treatment instituted was the production of a vaccine, and the hypodermic introduction of gradually increasing amounts of the silk vaccine. The child was immune to artificial silk, such as rayon, rayon being a carbohydrate and true silk a protein.

LYMPHADENOMA MACROGLOSSIA. DR. M. S. FINK.

The patient, a boy, was presented with a condition that his mother said had existed since birth. His tongue was enlarged to three times its normal size, there was a foul odor to the mouth, with a few vesicopustules about the left side of the tongue, in addition to a swelling of the left side of the neck, which also had been present since birth. On investigation the conditions of the tongue and neck proved to be lymphangioma. There was also an associated glossitis, which

accounted for a good deal of the swelling. The treatment has been irradiation, of which he was given some filtered x-rays on the right and left sides of the tongue; the dorsum and under surfaces were then irradiated, which reduced the swelling of the tongue to at least half its size within two weeks' time. The treatment for lymphangioma is irradiation, preferably with radium.

DEXTROCARDIA. TRANSPOSITION OF VISCERA. DR. MILA PIERCE.

On examination it was found that the patient, a boy, had a dextrocardia with complete transposition of all the viscera. The apex beat was visible in the right interspace, and the liver was palpable below the left costal margin, with the spleen beneath the right costal margin.

It is interesting that dextrocardia was discovered by an anatomist about 1600, but was not noted clinically until 1824, at which time auscultation came into use. Since that time about 400 cases have been recorded in the literature. This does not give an accurate idea of how frequently it is found, but it is apparently a rather rare condition. At the Mayo Clinic this condition was found in ten of a total of 347,000 cases. At the anatomic laboratory at Columbia University, New York, one case was found in the examination of 10,000 subjects. The etiology was vague, but the condition apparently was determined early in the development. In the interesting research of Speman, 1906, and of Pressler, 1911, on vertebrate embryos, in which a square of the medullary plate with a portion of the primitive foregut was rotated 180 degrees so that the original cephalic end was placed caudally, it was found that a number of these embryos developed complete viscus inversus.

TUBERCULOUS PERITONITIS. DR. G. E. BAXTER.

The patient, a girl, aged 5 years, was presented as evidence of poor prognosis given a year or more before presentation. She was presented at that time as having a case of tuberculous peritonitis, with probably a generalized tuberculosis. She has gone on to almost complete recovery. She had an extremely large, protuberant abdomen, and a pronounced anemia. She was seen by Dr. Baxter when she was 18 months old. When I first saw her there was a history of diarrhea of six months' duration, with blood in the stools during that time. During the next several months she had numerous infections, including otitis media and a mastoid, on which an operation was performed. A pronounced anemia developed. At one time the hemoglobin was only 10 or 15 per cent. She received an intraperitoneal transfusion while at the hospital, with a satisfactory reaction; later, blood was injected into a vein, and she collapsed. Afterward, she was given intramuscular injections and reacted favorably; she gained slowly but steadily. At no time was the hemoglobin about 51 per cent, and at the time of presentation it was about 40 per cent. There was blood in the stools for almost a year, and repeated examinations failed to disclose the cause. Skin tests were all negative for tuberculosis, and roentgenograms of the chest were normal. There was a question at one time as to whether the child was developing Addison's disease despite the extreme rarity of the condition during childhood. When previously presented she had the appearance of a patient with Addison's disease, but at the time of presentation the skin was more or less normal except for pallor. She gained in weight, ate well, had no abnormal symptoms and appeared to be making an excellent recovery. This case was one of tuberculous peritonitis, but no satisfactory explanation was found for the protracted diarrhea with blood in the stools.

EMPHYSEMA (SUBCUTANEOUS). DR. G. E. BAXTER.

The patient, a boy, was brought to my office a few days before presentation with marked swelling of the lower part of the face, neck and chest. It was evident that there was air in the subcutaneous tissues, but at the time of presentation this had almost disappeared. The history stated that in the summer of 1927, the boy had an attack of whooping cough which lasted for several weeks, and

that since that time he had repeated attacks of bronchitis. These attacks must have been of asthmatic nature. During the past few weeks, he had an acute attack, which was always worse at night. Previous to this he had not coughed any harder than before, but one night his mother noticed a swelling in the "glands" of the neck. It was a case of subcutaneous emphysema, brought on by rupture of either lung tissue or air vesicles on the surface of the lung. Dr. Baxter had never seen a case of this kind, which occurred during the course of an acute respiratory infection. In reviewing the literature he found that the prognosis was usually bad. The child showed constant improvement after being taken to the hospital, and at the time of presentation nothing was evident that caused apprehension. He was not sick, but had a low grade temperature. He received sufficient codeine to control the coughing, which probably had something to do with sealing the opening — wherever it was. Roentgenograms of the chest were negative for a tuberculous lesion, and the reaction to Pirquet test was negative, but the presence of air in the tissues was most evident.

CONGENITAL MALFORMATION (HEMIHYPERTROPHY). DR. MARTIN ZEISLER.

A girl, aged 5 years, showed a rather rare congenital malformation (hypertrophy of the left side). The asymmetry of the two halves of the body was complete, but was more marked on the face, trunk and upper extremities than on the lower part of the body. The x-ray pictures of the small bones of the metacarpus showed that the ossification was considerably advanced on the hypertrophied side. The child also had congenital glaucoma of the right eye, with cataract. There was a loud systolic murmur over the precordium, but no cyanosis. The child was mentally alert, but tired easily. The parents were well and had a younger child who was normal.

SINUS INFECTION. DR. CHARLES SCHOTT.

The patient, a girl, had eczema and asthma in infancy, from which she had been completely free for the past year or so. In May, 1928, she was seen two or three times with a respiratory infection, and on May 28 there was tremendous swelling in the region of the antrum. It was thought to be an acute sinus infection, and she was taken to the hospital immediately. The antrum was drained and pus found. Her temperature remained high from the time of her entrance to the hospital, and shortly after the first operation she developed an abscess on the septum, which was opened. Later, an abscess formed in the temporal region, which had to be drained. She was in the hospital for more than two months, was still under treatment and pus still discharged from the ethmoid sinus. The entire condition was due to a staphylococcus infection, and she was in desperate condition on two or three occasions. The tests on the blood and spinal fluid were negative. An autogenous vaccine was made, of which she received several doses. She also received quartz light therapy, because of her long stay in the hospital. In the roentgenograms it was interesting to note that the orbit showed the effect of an osteomyelitis. The otologist reported that the infection apparently broke through the ethmoid and antrum along the upper border of the orbit. Drainage was being done day by day, which seemed to be all that could be done for the fulminant sinus infection.

EMPYEMA (TREATED BY ASPIRATION). DR. E. T. MCENERY.

The three children presented, represented twenty-seven or twenty-eight consecutive cases of empyema in which the patients had been treated here during the past year, all by means of aspiration. Either a 50 cc. Luer syringe, with a 17 bore needle, or a special apparatus of vacuum type was used. The amounts of pus that were aspirated varied from 5 or 6 cc. to 2 liters. The amounts aspirated at one time varied, 800 cc. being the largest. The number of aspirations also varied, sometimes only two, sometimes eight or nine being necessary. Treatment was not made according to any routine, but depended on the clinical symptoms and signs which the child presented.

The cultures were rather interesting. In twenty-two cases pneumococcus was found, both on smears and on culture. Hemolytic streptococcus was present in two, *Staphylococcus albus* in one, and there was no culture in one case, for the child developed spontaneous pyopneumothorax, which condition cleared up. In one case, after more than 400 cc. of pus had been aspirated the patient was sent to the surgeon; however, the results that persisted in this case raised the question whether aspiration would not have done as well. Surgery was resorted to in this case because the heart was over to the right and did not come back as quickly as it should. The pus also seemed to pocket, and only 5 or 6 cc. could be removed at a time. One fatality occurred in a child who was taken away from the hospital against advice.

The children presented a similar clinical picture. They were all extremely ill after an attack of pneumonia; after aspiration was begun the general condition improved. At no time were they extremely toxic or did they run a septic temperature. All had gained in weight, and had practically normal chests. The children were seen every two or three months since early in 1928 in order to check the observations. Other physicians saw them, and they all agreed that it would be difficult to tell on which side the pathologic condition obtained. Roentgenograms were taken, which showed the condition at various times, and the gradual change that had taken place was plainly evident in the striking graphic records. On physical examination, the lungs were practically normal, with perhaps a slight suppression of breath sounds on the side on which aspiration was done.

In the first case, 495 cc. of pus was removed in seven aspirations, over a period of six weeks. In the next group small amounts of pus, anywhere from 2 to 10 cc., were removed, although clinical signs of pneumonia and empyema developed later.

Case 1.—A child, aged 6 years, showed no deformity of the chest. The results of physical examination were practically negative.

Case 2.—The patient developed pneumothorax, and whether this developed spontaneously did not seem to make much difference. This child developed spontaneous pneumothorax, and no aspiration was made following the onset. About 655 cc. was aspirated in six aspirations. Pneumothorax occurred, and the fluid persisted for some time, but there was no deformity of the chest, her appetite was good and she did not cough.

Case 3.—The patient was so ill that Dr. Brennemann was afraid to present her to the surgeon. It was seen that the chest appeared to be normal.

From this series the results to the time of presentation were gratifying. The ages of the patients varied from 2 to 10 years.

DISCUSSION

Dr. Brennemann: We are not recommending this treatment, but think we would rather have aspiration than surgical intervention, especially in young children.

Empyema. Dr. James H. Wallace.

The patient, a boy, aged 2 years, became ill on June 3, 1928, with a violent pneumonia involving the whole left lung. A week after onset pleural fluid was suspected, and on June 14, aspiration was done on the left side of the chest, and 10 cc. of thin milky-tinged straw-colored fluid was withdrawn. The fluid contained hemolytic streptococci. The child had a septic temperature, and the observations on the chest, typical of empyema, persisted. On June 26, another aspiration was done, and 60 cc. of pus, somewhat thicker than the first, was withdrawn. On June 27, the patient passed three copious stools mixed with cherry red blood and pus. Similar stools were passed for several days. Rapid improvement followed, the temperature becoming normal for the first time on June 29. On July 4, there began to be a rise in temperature again in the afternoon. On July 11, the patient vomited copiously what the mother described as pus. The temperature promptly became normal, and recovery was uneventful.

This apparently was a case of empyema which burrowed through the diaphragm, ruptured into the colon and drained by that route, later draining via a bronchus, with recovery.

SARCOMA OF KIDNEY. DR. HERMAN L. KRETSCHMER.

The patient, aged 7 months, was one of a series of four with interesting cases seen in the Children's Memorial Hospital within a period of eight weeks. When the child was 4 months of age the mother discovered a lump in the abdomen, which was about the size of an egg and which increased in size. It was diagnosed as impacted feces and enemas were advised, which made no change in the abdominal tumor. The question of the origin of the tumor came up. Various gastro-intestinal studies were made, and a diagnosis of retroperitoneal tumor was made, in all probability tumor of the kidney. There was no longer any reason why cystoscopy should not be performed on these children and why ureteral pyelograms should not be made, as in adults. Cystoscopy was performed on this patient, but the genital tract was so small that catheterizing cystoscopy could not be used. In such cases, there is an advantage of indigo carmine, and the function was studied in this way. It was found that the child had a large, hard, solid tumor, which came out from under the arch of the ribs. It was exceedingly hard and nodular and projected beyond the level of the chest. The lower margin came to the symphysis, and extended on the right to the anterior posterior spine.

There were two or three conditions to consider — retroperitoneal sarcoma beginning in the lymph nodes, sarcoma of the kidney, hydronephrosis, and possibly, on account of the irregular character of the tumor, tuberculous peritonitis. After the studies made by Dr. Brennemann and his associates and the changes seen around the ureteral orifice, the condition was considered sarcoma of the kidney, or a mixed tumor.

The interesting fact about these cases has always been the enormous size of the growth. The patient had an enormous tumor of the abdomen, which was discovered by the mother in an accidental way. In children, some of these tumors run about the same course as in adults. Many of the patients have fever. A case like this seems to be a hopeless problem. In one of the four cases in this hospital the tumor was definitely inoperable. Some sections were removed for study, and they showed a villous (?) tumor. In the second case, the tumor was removed. The third case, again, was inoperable, and sections were removed for study. The case presented was the fourth case. In two of the cases resort was had to deep roentgen therapy. In one case there had been a cessation of the growth of the tumor, and perhaps a slight decrease in size. It was impossible to show the other patient. In that case the tumor was much larger than the one presented, but after eight or nine deep roentgen treatments it was not more than one-fourth its usual size. At times deep roentgen therapy will do this, and if not proved by histologic study one questions the diagnosis. In this instance all of the observation coincided, and the diagnosis of sarcoma was made. Whether the other fourth of the tumor will disappear, or whether the child will have metastases was not known, but the results to the time of presentation were gratifying. If all these patients were treated with deep roentgen therapy, it would give the patient an added safety. Most patients go to a fatal termination, no matter whether they are operated on early or late.

TWO CASES OF SYPHILITIC LARYNGITIS. DR. HAROLD A. ROSENBAUM.

Syphilitic laryngitis is rare in infancy and childhood. There have been two cases in the clinic of the Children's Memorial Hospital. The first was that of an infant, aged 1 year, who was taken to the clinic because of aphonia of six weeks' duration. He had a typical syphilitic facies, and rhagades, cross-ridging of the nails and large epitrochlear nodes were present. There was a history of snuffles and the loss of all the nails of the fingers and toes. The Wassermann and Kahn reactions of the mother and child were 4 plus.

At the time of admission the laryngoscopic examination was as follows: "The larynx is swollen, especially the arytenoids. The epiglottis is swollen and thickened. The mucosa bleeds easily."

Treatment was instituted, giving the infant, who weighed about 15 pounds (6.8 Kg.), 0.1 Gm. of sulpharsphenamine every five days and potassium iodide, 2 grains (0.13 Gm.), twice daily, increasing the amount 1 grain (0.06 Gm.) daily to the end of a week and then returning to the original dose and similarly increasing the dosage.

One week after treatment was instituted, this clinical note appeared on the chart, "baby distinctly better, cries aloud at times." Two days after the note, the following note appeared, "gaining weight steadily, almost a normal cry." The child was discharged from the hospital at less than one month after admission, and this note appeared, "The epiglottis is practically normal. The posterior part of the larynx is almost normal. There are no bleeding areas and the vocal cords move freely."

The second case was that of a boy, aged 11 years, whose history of voice difficulty went back about one year previous to admission. For about six months he was hoarse, and then for about six months was entirely voiceless.

There was no condition suggestive of syphilis, except the high, prominent, frontal bosses. These were, of course, found in other children who have had high grade rickets, but they were so often seen in syphilitic children that it was believed that their presence indicated serologic tests for syphilis.

The Wassermann and Kahn reactions were 4 plus. The initial laryngoscopic examination showed, "Both cords roughened and red, especially the right. There is swelling and redness of the false cords and some thickening of the epiglottis." Treatment was begun August 16, with sulpharsphenamine and with potassium iodide, 5 grains (0.97), thrice daily. On September 6, the boy could use his voice although it was husky. He continued to improve, although with the chronicity of the lesion it will probably be sometime, if ever, until the voice is perfectly clear.

NEUROLOGIC CASES. DR. BERT I. BEVERLY.

CASE 1.—*Cerebellar Tumor.*—A white girl, aged 9 years, was well until three months before presentation, at which time she developed frontal headache and projectile vomiting. The latter was without provocation but increased by change in posture. With the increasing severity of these symptoms she developed dizziness and weakness and became bedridden in a few weeks. On entrance to the hospital four weeks before presentation, she had severe frontal headaches, vomiting and markedly choked disks. There was dizziness at times. She was extremely weak and markedly emaciated. There was rigidity of the neck, but little tenderness or difficulty in rotation of the head. The deep reflexes could not be elicited. There was diplopia in the right eye. There was little lateral movement of the eyes but no difficulty in vertical movements. The observations at the time of presentation were the same as on entrance except that they were more pronounced. The headache, vomiting and choked disks suggested increased intracranial pressure and tumor. The dizziness, weakness and rigidity of the neck spoke for posterior fossa—cerebellar tumor. The observations on the eye apparently indicated pressure on a part of the nucleus of the third nerve. Operation by Dr. Loyal Davis was contemplated in a few days. (Subsequent autopsy before operation revealed a tumor involving the middle and right lobes of the cerebellum.)

CASE 2.—*Functional Vomiting and Purulent—Hemorrhagic Encephalitis.*— A Jewish girl, aged 9 years, who was critically ill, was first examined in the outpatient department seven months before presentation. There was a history of vomiting, from one to three times a day, and abdominal pain nearly every day, when she would lie in bed, hold her abdomen and scream for one or two hours at a time. These symptoms were present for about two years and were progressing. Her tonsils and appendix had been removed, without improvement of the condition. She was placed in the hospital for two weeks' observation. The results of the examination, including neurologic and gastro-intestinal studies, were entirely nega-

tive, and the vomiting and the abdominal pain disappeared. Her mother died when the patient was 2 years old. Since that time she had been forced to eat and was cared for by an unstable, unsympathetic grandmother, who gave her poor food and criticized her a good deal. It was thought at that time that her condition was purely functional. She returned to the clinic two months before presentation. The vomiting and abdominal pain were worse; she was extremely emaciated, weighing 37 pounds (16.8 Kg.), had a hemoglobin of 40 per cent and appeared ill. She had been in the hospital since that time. She vomited on two occasions, and both times it was induced by putting her fingers down her throat. She ate fairly well and did not complain of abdominal distress.

Very large adenoids were removed ten days before presentation. Recovery was uneventful and she did well until two days before presentation, when she vomited at 5 a. m. and went into deep coma. In a few hours her temperature rose to 103.5 F. and had been high since, being 104.8 F. at the time of presentation. In addition to the deep coma, on Nov. 19, 1928, she had a marked spasticity of the left side, with bilateral Babinski, Gordan and Oppenheim signs. At the time of presentation she had a marked rigidity of the right side and some of the left. There was moderate rigidity of the neck. The eyegrounds were somewhat pale. The cranial nerves were otherwise apparently normal. A spinal puncture revealed 300 cells with a sugar content of 110 mg. It was believed that she had a severe meningo-encephalitis, and that the present condition was not related to her previous symptoms except that her general run-down condition was probably a contributing factor. (Autopsy three days after the onset of the acute condition revealed an extensive hemorrhagic and purulent encephalitis, involving, macroscopically, the lateral ventricles, internal capsules and adjacent structures.)

Case 3.—*Malignant Tumor of the Spinal Cord.*—A Polish boy, aged 5 years, was well until April, 1928, at which time he began vomiting, at first once a week, later more often, and without provocation. A few weeks later he had several generalized clonic convulsions and was taken to the Cook County Hospital. According to the parents, no cause for the convulsions could be found, and epilepsy was considered. In June, he had several more generalized convulsions. About the same time he complained of severe pains in the legs, which kept him awake at night. A few days later he was unable to walk and was taken to the hospital. At the time of admission he had a complete flaccid paralysis of the lower extremities, a cord bladder and complete anesthesia to a point corresponding with a lesion of about the fourth or fifth lumbar region. A Quackenstedt indicated a block between the fourth and sixth lumbar interspaces. Injections of iodized oil (40 per cent) demonstrated a complete block in the same region. When the patient was admitted to the hospital, the only history was of a fall; hence, the diagnoses of compression myelitis was made. A laminectomy was done by Dr. Loyal Davis about two months before presentation. He found a bloody extradural tumor, which was removed. As a tumor of the spinal cord often gives a picture of compression, a diagnosis of tumor could not have been made without the accurate history which was obtained after operation. There was no return of function at the time of presentation. A few days before presentation, the patient developed a respiratory difficulty. Roentgenograms showed extensive pathologic processes throughout the lungs, indicating a malignant condition. A report on the microscopic observations of the tumor had not been received. The origin of the malignant growth and cause of the convulsions had not been determined.

Brain Tumor. Dr. E. T. McEnery.

The patient entered the hospital during October, 1927, with signs of tumor of the brain. A decompression operation was performed by Dr. Loyal Davis, who advised deep roentgenotherapy. The child improved and went home, and deep roentgenotherapy was given at the Henrotin Hospital. The condition seemed to be improved, and the child was shown at the pathologic conference to demonstrate the good effects of the roentgen rays on tumor. He was taken back during the summer, because of difficulty in walking that necessitated hospitalization, and since

that time has remained there, being taken to Henrotin Hospital for deep irradiation. The condition, however, is becoming worse. At the time of presentation he had the clinical signs of emaciation and progressive wasting. No sections were made, but the process was a midline cerebellar tumor.

METASTASIS OF MALIGNANCY. DR. J. A. BIGLER.

During the past year three patients have been observed with a malignant condition which has metastasized to the mediastinum, giving a rather characteristic roentgenogram. Roentgenograms were taken of the chests of all patients with tumor to determine whether any metastasis had occurred. The mediastinum presented a bulging shadow which encroached on the lung fields and had a convex, scalloped border. On necropsy, this proved to be caused by a marked enlargement of the mediastinal lymph nodes due to metastatic involvement. In only one case was there metastatic involvement of the lung tissue itself.

CASE 1.—*Localized Pneumothorax.*—A boy, aged 2 years, was admitted to the hospital with otitis media and pneumonic consolidation of the lower lobe of the right lung. Three weeks later, roentgenograms showed a honey-comb appearance in this area which gradually developed into a rounded area of decreased density. The consolidation disappeared, and the area of decreased density increased in size so that at the time of presentation it involved nearly the entire lower half of the right side of the chest, being surrounded by a thin ring of increased density with smooth margins as seen on the films. There were no lung markings, and at no time was there a fluid level. An injection of iodized oil (40 per cent) was made into the main lower branch of the right bronchus under ether anesthesia. Iodized oil was not seen in the area of decreased density, but could be seen in the bronchi medially and above. This condition was diagnosed as localized pneumothorax which had increased to its size at the time of presentation and showed no evidence of infection. The physical observations early were those of pneumonia, but at the time of presentation, there was only slight hyperresonance, and faint breath sounds could be heard. The pneumothorax had been its size at the time of presentation for about two months, and the child appeared perfectly well.

CASE 2.—A child, aged 2 years, was admitted to the hospital with an empyema of the left side of the chest, and later developed an area of consolidation in the upper lobe of the right lung. A week later, a rounded area of decreased density was found by roentgen rays at the site of the pneumonia. It was sharply limited by a thin line of increased density with smooth margins. Its largest size was about that of a dollar. Physical observations were never present. It began to decrease in size and completely disappeared after about three months. The empyema of the left side had completely healed. The boy appeared to be healthy, and the roentgenogram of the chest was normal. The condition was diagnosed also as localized pneumothorax.

CASE 3.—*Chronic Tuberculous Bronchopneumonia.*—The patient was shown because of the marked roentgen observations as compared with the general good health of the child. He was 2 years of age, and was admitted to the hospital in May, 1928, with a history of cough. The results of a physical examination of the chest were negative. The roentgenograms showed a deformity of the spine due to Pott's disease and a marked pathologic condition of the chest. It was at first thought to be miliary tuberculosis, but the child had remained in such good condition that it is thought to be chronic tuberculous bronchopneumonia. The only physical observations have been occasional râles and occasionally slight dulness in the lower lobe of the right lung posteriorly. The Pirquet sign was markedly positive, and the patient was afebrile most of the time. There was bilateral involvement, and the shadows on the film were larger than those seen in miliary tuberculosis. During the six months prior to presentation there was practically no change in the shadows, and the child was well nourished and in apparent good health, except for Pott's disease. No calcifications were present; the Wassermann reaction was negative.

CONGENITAL HEART DISEASE. BRONCHITIS (ASTHMATIC). DR. GUSTAV KAUFMANN.

The patient was a twin whose twin was taken to the hospital first on April 13, 1928, because of a congenital heart and asthmatic bronchitis. The twins were born on Nov. 23, 1927. The patient's twin, a girl, was treated in the outpatient department until Sept. 19, 1928, at which time she entered the hospital because of cough, vomiting and cyanosis which had begun six days previously. There was extreme dulness over the entire left side, absent breath sounds and a loud, blowing, systolic murmur. The border of the right side of the heart was midsternum. A diagnosis was made of collapsed lung and congenital heart disease. The child became progressively worse, developed a high temperature and cyanosis, and death occurred on Oct. 6, 1928, seventeen days after admission.

Necropsy revealed a fetal endocarditis, with fibrous thickening and stenosis of the mitral and tricuspid valves, a patent ductus arteriosus, complete atelectasis of the left lung and extensive hypostatic pneumonia of the left lung.

In the family history it was found that the mother during pregnancy had a severely ulcerated tooth and an attack of so-called streptococcic sore throat. The family physician corroborated this history.

In view of this history, the patient was taken to the hospital eight days after the admission of his sister. At that time he had cough, fever, loss of weight and vomiting. On examination crepitant râles and a congenital condition of the heart were found, with the border of the right side of the heart midsternal, dulness of the entire left side, and diminished breath sounds. It was evident that the heart was being pulled over and that there was a progressive collapse of the left lung, similar to that which existed in the twin. The roentgenogram verified these observations. It was not pneumonia but a complete collapse of the lung.

The diagnosis in this case, based on the observations and necropsy on the twin, was fetal endocarditis, plus a congenital defect and collapse of the lung.

DUODENAL ULCER. DR. C. A. ALDRICH.

CASE 1.—A child, aged 7, was first seen at the age of 1 year, with severe whooping cough and pronounced anorexia. The anorexia had persisted for six years, in spite of tonsillectomy at the age of 4 years. In February, 1928, Dr. Aldrich was called to see the child because of a stool which the mother reported "looked like coal." The next day blood was found in the stools. The history was not that of ulcer, but because of blood in the stools a roentgen examination was made, which showed a marked defect in the duodenal bulb, and considerable delay in the emptying time of the stomach, so that a diagnosis of duodenal ulcer was possible. The child was placed on a modified Sippy management, with the addition of atropine; the deformity of the duodenal bulb improved markedly, as was shown in the roentgenogram.

The interesting part of this case was that the roentgenograms taken five hours after the barium meal showed retention of about two thirds of the meal, and each picture showed decreasing amounts of retention. It was interesting to speculate whether the child had an infantile ulcer, which had been present since birth, causing the gastric delay and hence the anorexia. The physician who cared for the child during infancy expressed a desire for a roentgenogram of the stomach. The child gained weight rapidly on treatment, and the anorexia was almost cured.

CASE 2.—*Osteogenesis Imperfecta.*—Dr. Aldrich was called to see the patient, an infant, by a physician who said he had broken the leg of the infant in a breech delivery. The left leg was in a temporary splint, and the heel of the right leg was in the axilla. The head felt more like a Charcot joint than anything else. The occipital bone was "mushy." X-ray examination demonstrated that both legs were broken. There was a peculiar shortness of the femurs that made one think of achondroplasia. The skull showed innumerable areas of rarefaction. Both humeri were fractured in utero, but these fractures had healed. The child was gaining rapidly, and the fractures were healing. The prognosis, however, in this disorder is worse in the congenital cases.

DIETARY TREATMENT FOR NONSURGICAL PYLORIC STENOSIS. DR. L. W. SAUER.

Evidence collected during the past four years led to the tentative conclusion that the volume of a feeding was more important than the consistency of the food. Although a relatively high percentage of patients recovered on thick cereal feedings, starch was not a physiologic food for the young infant. Such feedings were time consuming, especially when infants refused to swallow the thick food, and intercurrent fevers were wont to develop if the consumption of water was inadequate. The food must be of high caloric content, readily digestible and free from coarse curd formation while in the stomach. The volume of a feeding must be less than that which elicits the vomiting reflex.

Preliminary in vitro tests were made with 30 cc. of various milk mixtures. After 7.5 cc. of 0.5 per cent hydrochloric acid (containing 0.5 per cent pepsin) had been added, the mixture was placed in the incubator for four hours. This, in a crude way, simulated gastric digestion. Raw cow's milk produced large curds like those described in Dr. Brennemann's gastric experiments; boiled milk separated into whey and somewhat finer curds; farina cooked in half milk (1:7) was firm and colloidal; breast milk and a mixture of powdered milk and powdered protein milk in water formed finer curds than those of the boiled milk, and diluted evaporated milk produced extremely fine curds.

Since 1924, various small, concentrated, liquid feedings have been tried in twelve cases of pyloric stenosis. An attempted standardization led to two formulae which might be adjusted to the individual case:

Formula A. Powdered milk, 7 (or 5) level tablespoonfuls
Powdered protein milk, 7 (or 5) level tablespoonfuls
Soluble carbohydrate, 3 level tablespoonfuls
Water (or breast milk), 10 ounces (283.50 Gm.).

(When breast milk is available the lower figures are used.) The caloric value approximated 50 calories per ounce. It may be fed by bottle, Breck feeder or dropper, as the consistency is that of rich cream. At first ½ ounce (14.17 Gm.) is given seven times in twenty-four hours; after a day or two 1 ounce (28.35 Gm.) is given at a time; a week later it may usually be increased to 1½ ounces (42.52 Gm.); when vomiting has completely ceased 2 ounces are usually well tolerated. One-fourth grain (16 mg.) of phenobarbital in from 1 to 2 ounces of tap-water or Ringer's solution should be given by retention an hour before feeding, three or more times daily, or 75 cc. of dextrose Ringer's solution may be given by hypodermoclysis once or twice daily. In the latter case, 0.25 grain of phenobarbital may be added to two or more of the feedings. After a fortnight of cautious feeding, from 1 to 3 drachms of water may usually be given several times a day, even in extreme cases, without causing projectile vomiting. This type of formula was successful in six of eight cases.

The work of Drs. Dick, about a year ago, on the bacteriology of powdered milks, led to the adoption of breast milk enriched with evaporated milk and soluble carbohydrate. If breast milk is not available, water may be used.

Formula B. Evaporated milk, 5 (or more) ounces (141.75 Gm.)
Soluble carbohydrate, 1 (or more) ounces (56.70 Gm.)
Breast milk (or water), 7 (or more) ounces (198.45 Gm.).

If this formula is boiled, enough sterile water should be added to total the initial amount. The caloric value varies according to the proportions of the ingredients used, but should be at least twice that of breast milk. The quantity, time interval, water and phenobarbital are as previously described. The formula has been used with excellent results in four successive cases.

Chart 1 gives the weekly weights of a patient with a severe case who recovered on powdered milks formulas. Chart 2 is that of a patient with an incipient case who was fed the more recent formula. X-ray pictures of each (before treatment was begun) showed marked gastric retention at the end of five hours. Both showed peristaltic waves after feedings during the first months of convalescence.

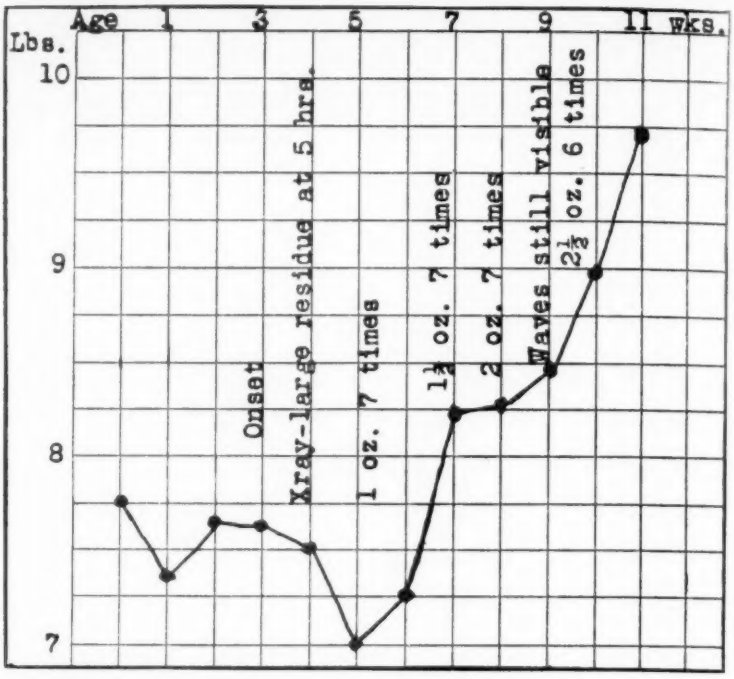

Chart 1 (case 1).—Weekly weights of patient with severe case of pyloric stenosis, fed formula A.

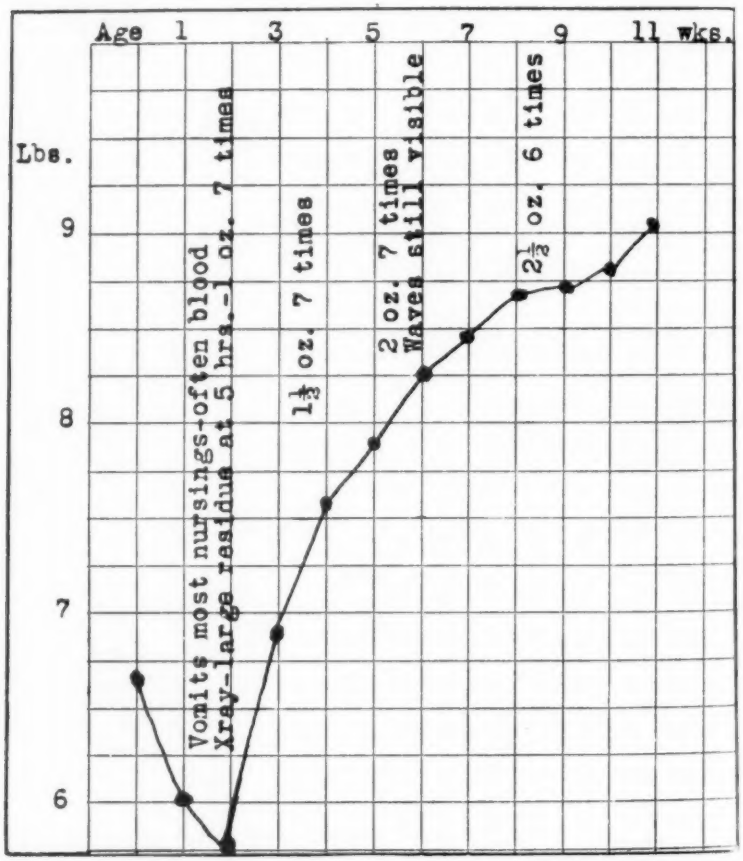

Chart 2 (case 2).—Weekly weights of patient with an incipient case of pyloric stenosis, fed formula B.

Dr. Sauer came to the following conclusions: 1. The volume of a feeding should be below that which elicits the vomiting reflex. 2. The amount of food retained (passing the pylorus) should be ample to insure a consistent weight increase. 3. Sufficient water should be furnished routinely by avenues other than per os. 4. One grain (or less) of phenobarbital daily seems to aid in the relaxation of the pyloric sphincter. 5. The earlier suitable, small, concentrated feedings are instituted, the less likely will surgical intervention be necessary.

ENLARGEMENT OF THE HEART (CONGENITAL). DR. MILO MILLER.

An infant, aged 11 days, was seen on account of an apparent difficulty in swallowing. The chief interest in the case was the symptomatology. The child was normally formed but had never nursed well, had a weak cry and signs of cyanosis, which became extremely marked when the infant attempted to take food. Almost constant aspiration with a tonsil aspirator had to be carried out in order to prevent asphyxiation at feeding time. Congenital stenosis of the esophagus was considered, so a catheter was passed and a small amount of barium given. The roentgenogram showed an enormous heart, with the enlargement apparently predominant in the right side of the heart, which pushed the esophagus backward. The day following this examination the child died, and necropsy revealed a heart which occupied nearly the entire cavity of the chest. There was no aorta. A single large vessel made exit from the right ventricle. The only blood supply that went to the lungs was from a large vessel which opened from the side of this large vessel. The symptoms of esophageal obstruction were due to the enormously dilated heart.

EDEMA OF HEART FAILURE IN CHILDREN. DR. HARROLD A. BACHMANN.

In cardiac work with children, there have been observed two types of edema associated with heart failure. The first type is the generally accepted cardiac or dependent type. This edema is usually seen in the more chronic varieties of involvement of the heart. The second type is generalized and is not unlike that seen associated with nephritis. That this variety, when occurring with heart failure, is not renal in origin has been sufficiently proved by the constantly negative results obtained from the customary examinations on the urine and blood.

The two types are further established as clinical entities by their constant clinical course and also by the therapeutic agents to which they respond. With the dependent type, digitalis in large amounts is necessary. If no response is observed, abdominal paracentesis and the strong mercurial diuretics are necessary. In the second or generalized type, digitalis has little or no effect even if given to the point of digitalization. Theobromine sodium salicylate, however, acts almost as a specific.

Regarding the clinical course, it has been observed that when the patient with dependent edema does eliminate with a resulting loss of weight, no systemic reaction is noted. When, however, the patient with generalized edema shows a response with a decreasing body weight and increased elimination, a marked rise in temperature with toxic symptoms are noted. This has led to the conclusion that the origin of the edemas differs in spite of the fact that they both occur in the heart failure of childhood.

The conclusion drawn was that the dependent type of edema is chiefly of circulatory failure with stasis and a resulting edema. In the cases of generalized edema it does not seem probable that stasis is an important factor. Because of the generalized character, it seems logical to conclude that the cause of edema may be largely toxic. If edema is a protective mechanism as suggested by Aldrich, the withdrawal of the diluent might concentrate these hypothetic toxins and account for the symptoms encountered here. This sequence of events has so frequently repeated itself during these observations that the hypothesis seems likely.

PRESENTATION OF PATHOLOGIC SPECIMENS. DR. I. M. EPSTEIN.

Six tumors of the brain in children under 3 years, three abscesses of the brain and one tuberculoma have been seen. In the past eight months there were four tumors of the brain. With one exception they were cerebellar, midline, infiltrating, of the glioma type. The study has not been completed in all the cases. Cerebral abscess is comparatively rare in children under 10 years. Thirty-two cases are recorded, including two in children under 10 years, and four of the cerebellum in children under 1 year of age. Two cases have been seen in children under 1 year of age within the past year, which led to the thought that perhaps the condition is not so rare as the literature leads one to believe.

Of the cases reported, staphylococci were found in nine of ten cases in which culture was taken. In the cases reported, in two instances *Streptococcus hemolyticus* was found, in one a staphylococcus and in one case a colon bacillus. The cerebral abscess in one instance occurred in a child, aged 8, who had been seen in the clinic since the age of 2. The case was first diagnosed as a "congenital heart." When seen later all of the clinical symptoms of a congenital malformation of the heart were present. The child subsequently developed a rheumatic fever, with rheumatic joints, and it was decided that she had, superimposed on the congenital heart, a rheumatic infection. Tonsillectomy was performed in a quiescent interval, and four days later she suddenly developed generalized convulsions, and for the rest of the day was drowsy. The drowsiness persisted the next day, but there was no localizing sign. On the eighth day following tonsillectomy, she first showed a definitely stiff neck and positive Kernig and Babinski signs, and a diagnosis of meningitis was made. Examination of the spinal fluid revealed 5,000 cells. One day before death occurred she developed localizing symptoms, and at necropsy an abscess was found, which had ruptured, spread out over the side of the temporal lobe and caused meningitis. The histologic observations were not sufficient to make certain that the abscess had been there for an extended period.

In the past eight years only one tuberculoma has been seen in the clinic, which is contrary to the older opinion that tuberculoma is the most common intracranial tumor of childhood. The cases presented represent the incidence in more than 900 autopsies, in 121 of which there was a tuberculous infection.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Regular Meeting, Jan. 10, 1929

STAFFORD MCLEAN, M.D., *President, in the Chair*

THE RÔLE OF FOCAL INFECTIONS IN THE PRODUCTION OF GASTRO-INTESTINAL SYMPTOMS IN INFANTS AND CHILDREN. A. CLINICAL ASPECTS. DR. MCKIM MARRIOTT.

In the nutritional disturbances of infants characterized by progressive loss in weight or acute gastro-intestinal symptoms of vomiting and diarrhea, suitable food often fails to bring about improvement in the condition. In these cases there is likely to be evidence of infection as shown either by irregular temperature or leukocytosis or by both. In a certain number of instances, a history is obtained of an infection of the upper respiratory tract preceding the onset of the nutritional disturbance. This may have been an acute infection which had apparently subsided, although careful examination often reveals evidence of a low grade infection of the middle ear. The ear drum may not be red or bulging but may have lost its luster and have a dirty gray appearance. In some instances free paracentesis results in improvement in the nutritional condition, but in other instances only slight or

temporary improvement occurs, and the infants ultimately succumb to the nutritional disturbance. A common observation at autopsy in these infants has been pus in the mastoid antrum, which has become walled off from the tympanic cavity by obstruction at the aditus. This observation was first made by du Verney in 1684. In 1921, Renaud reported finding pus in the mastoid antrum at autopsy on seventy young infants who had died of nutritional disturbances. Byfield and Dean and Floyd reported similar cases. Since 1923, I have opened the mastoid antrums of young infants at autopsy as a routine and have frequently observed evidences of infection. The question arose as to whether the infection present was the cause of the continuance of the nutritional disturbance or merely a terminal complication. If it is a cause, operative drainage should be expected to effect improvement. Operation was accordingly performed in a number of severe cases presenting the symptoms of progressive athrepsia or the symptom complex usually referred to as "alimentary intoxication" with acidosis and dehydration. Striking improvement was frequently observed which could not be referred to other methods of treatment. In all cases evidences of otitis media were present, and paracentesis had been performed, usually repeatedly. There were also otologic evidences of antrum suppuration, the most striking of which was a bulge of the posterior superior portion of the ear drum and adjacent canal wall. In none of these cases was any redness, tenderness or swelling apparent externally over the mastoid region. The operation was performed under local anesthesia, according to the method described by Alden. A small button of bone was removed over the antrum and a drain inserted. It was found inadvisable to perform curettage, but a probe was usually inserted through the aditus to render it patent.

The organism most frequently found from cultures of the mastoid was a hemolytic streptococcus. A considerable number of the strains obtained from mastoids were found to be toxin producers, as shown by a positive skin test with the filtrate in high dilutions. The toxin was neutralized by convalescent scarlet fever serum. Of thirty-six patients operated on from whom the hemolytic streptococcus was obtained on culture, thirty recovered, the mortality being 16 per cent. The organisms occasionally found were the hemolytic streptococcus pneumococcus and *B. pyocyaneus*. The cultures obtained from the mastoids did not necessarily correspond with those obtained from pus from the middle ear. All of the foregoing cases were those in which there had been previous evidence of rhinopharyngeal infection.

A second group of cases presented a different clinical picture. In these, the evidence of preceding rhinopharyngeal infection was usually lacking. There was often a history of poor feeding followed by severe gastro-intestinal disturbances, vomiting and profuse watery diarrhea. The ear drums were rarely acutely inflamed or bulging, but as the disease progressed they became dull and thickened. The bulging of the superior posterior portion of the drum later became evident. Paracentesis usually yielded a thin, seropurulent fluid. Operation on the mastoids of these infants revealed an abnormal antrum, and from antrum cultures bacteria of the intestinal group were found, either *Bacillus coli* or *Bacterium morgani*, usually the former. A number of the cultures of the colon bacilli were tested by Dr. A. I. Kendall for histamine production and were found to be strong histamine producers, in this way differing from the usual organisms of the colon-typhoid group. Following antrotomy on these patients, improvement was not as quickly or as regularly observed as in the patient with streptococcic infections, although the operation seemed to decrease the toxemia somewhat and give the infant a chance to recover.

The clinical picture in these cases suggested that intestinal infection was chiefly responsible for the symptomatology and that the involvement of the ear was secondary but sufficient in itself, at times, to determine the fatal issue. There is considerable evidence to indicate that these cases are a true "alimentary intoxication" in contradistinction to the preceding group in which the gastro-intestinal symptoms are secondary to parenteral infection. There is evidence that the secondary mastoid infections due to the histamine producing intestinal organisms may be capable of aggravating the gastro-intestinal disturbance and bringing about

the toxic manifestations. Preliminary experiments with implantation of cultures in the antrum of animals have supported this view. The mortality in this group of cases, as would be expected, was higher than in other types, being 50 per cent in the cases in which operation was performed, which included only the more severe ones.

In the cases of the first group, in which the condition was due to the streptococcus and in which the gastro-intestinal symptoms were presumably secondary, it was not found necessary to resort to special methods of feeding. Recovery from diarrhea followed drainage of the antrum despite the administration of a liberal diet. In the second group of cases, presumably of primary alimentary origin, careful feeding was found to be essential; it was usually advisable to give only dextrin for a period and later, dextrin with skimmed lactic acid milk. In both groups frequent transfusions have been found of benefit, and administration of fluid has been necessary to combat the dehydration. Whether the fluid selected is saline or dextrose solution has depended on the changes in the blood chemical values and the presence of acidosis. With high blood chloride content and acidosis, dextrose has been found superior to saline. In the presence of acidosis, the administration of some bicarbonate in isotonic solution is theoretically indicated and has been followed by favorable results.

It is to be emphasized that only those patients with athrepsia or "alimentary intoxication" who have presented otologic evidences of involvement of the mastoid antrum have been operated on. These have usually been infants with the more severe forms of the disease. The others have been treated by the usual methods. Altogether, the operation of antrotomy has been performed on 118 infants. In those in which the hemolytic streptococcus was found, the mortality was 16 per cent and in those with intestinal organisms, 50 per cent. The mortality for the entire group, including infections with all types of organisms, was 33 per cent.

B. Chemical Changes in the Body. Dr. A. F. Hartman.

As a result of chemical study of the blood plasma and urine in cases of pyloric stenosis, intestinal fistula and obstruction, pancreatic fistula (dog), infections in the respiratory, intestinal and urinary tracts associated with vomiting or diarrhea, and in cases of experimentally produced "salt fever" and "intestinal intoxication," the following conclusions seemed warranted.

The changes in electrolyte, nonprotein nitrogen and total osmolar concentration of the body fluids, which are frequently found associated with focal infection giving rise to gastro-intestinal symptoms, depend not so much on the site of infection as on the quality and quantity of gastric, pancreatic and intestinal secretions lost by diarrhea and vomiting, and the extent to which urinary secretion compensates for such loss. Parenteral and enteral infections may lead to almost identical changes.

When severe watery diarrhea and oliguria persist, more fixed base than acid is lost from the body, and a relative base deficiency type of acidosis results. The actual concentration of fixed base in the plasma may be normal, high or low. Initially it tends to be high, falling to normal or subnormal if adequate restoration of urinary secretion occurs, but remains elevated or actually increases if inadequate urinary secretion accompanies the parenteral administration of large amounts of physiologic solution of sodium chloride or Ringer's solution. The changes in the concentration of individual anions and nonprotein nitrogen depend on such factors as loss of water from the plasma, total metabolic rate (particularly rate of catabolism of protein) and the degree to which circulation and renal secretion are impaired.

When vomiting results entirely or chiefly in the loss of only ingested food and gastric juice, more fixed acid than base tends to be lost, and a relative fixed acid deficiency type of alkalosis results. The actual concentration of fixed base may be normal, but usually is subnormal. When vomiting results in the loss of both gastric and intestinal secretions, a greater loss of fixed base relative to fixed

acid occurs and alkalosis is less severe, but dehydration and increase in nonprotein nitrogen concentration is usually more marked.

Anuria or oliguria associated with acidosis, while perhaps beneficial in that it causes no further loss of water and electrolyte from the body, is decidedly objectionable in that it prevents restoration of plasma and body fluid $BHCO_3$, by the secretion into the urine of unneutralized acid or acid bound to ammonia. From this standpoint, diuresis is a prime therapeutic indication. Because of its effect of driving out $BHCO_3$, salt solution administered parenterally is inferior to isotonic or moderately hypertonic dextrose solution, the effect of which, on urinary secretion, is practically that of pure water.

When acidosis is marked ($BHCO_3$ and p_H reduction), and particularly when it is associated with persistent marked diarrhea, dehydration, sclerema, elevation of chloride concentration and oliguria, restoration of $BHCO_3$ by administration of parenteral dextrose or salt solution may either be impossible or too slow to prevent death from acidosis. In such instances, the intravenous or subcutaneous administration of sodium bicarbonate solution properly prepared and in proper dosage may be a life-saving measure, the repetition of which, however, may be frequently necessary, if pronounced diarrhea persists.

When alkalosis results from the loss of gastric juice, urinary secretion is attended with no loss of the chloride ion and little loss of fixed base, both of which are reduced in the body fluids. The failure to excrete $BHCO_3$, despite its great elevation in the body fluids, accounts for the acid reaction of the urine in the presence of increased alkalinity of the plasma. When fixed base and chloride are administered, retention of both occurs until their respective normal concentrations are restored, when both are then secreted into the urine. Because of the relatively greater reduction of chlorine than boron, administration of physiologic solution of sodium chloride or Ringer's solution is attended first by restoration to normal concentration of fixed base; its secretion in the urine combined with the bicarbonate ion occurs early, increasing the alkalinity of the urine while reducing that of the plasma and body fluids. The administration of salt solution, therefore, is ideal in the treatment for this type of alkalosis.

The fact that combined loss of gastric and intestinal secretion by obstructive vomiting or fistula leads to some degree of alkalosis, while the combined loss of the same secretions as a result of vomiting and diarrhea secondary to infection usually leads to acidosis is perhaps explained by the diminution in secretion of gastric hydrochloric acid commonly observed during infection. Whether infection also affects the quality and quantity of pancreatic juice is at present unknown.

DISCUSSION

DR. RUTH C. SULLIVAN: I have been greatly interested in the papers by Dr. Marriott and Dr. Hartmann, more particularly in that by Dr. Hartmann, for my associates and I have also been studying the chemistry in intoxication.

Dr. Hartmann discussed the chemical changes in the body during primary or secondary mastoid infections in infants who presented the clinical picture of alimentary or intestinal intoxication. In a series of about 100 cases of intestinal intoxication we found normal ears in 37.5 per cent, while 62.5 per cent showed infection of the middle ear. In 12.5 per cent, no focus of infection was found. A variety of infections was manifested — bronchopneumonia, bronchitis, pharyngitis, cervical adenitis, osteomyelitis, impetigo, dermatitis, furunculosis and thrush.

In 90 per cent of our untreated patients, the chlorides were normal or above normal. We have found a remarkable constancy in the reciprocal relationship between the base bicarbonate and the base chloride of the blood. The lowest carbon dioxide combining power has been associated with the highest chlorides. In the rare cases in which on admission to the hospital the patients showed a decrease in blood chloride, the base bicarbonate was found to be near or within the normal limits. In disagreement with Dr. Hartmann, we found the chemical picture altered immediately on introduction of fluids into the body.

As Dr. Hartmann pointed out, theoretically the therapy is clearly indicated. The body has lost and is losing water and certain necessary salts, and this loss has resulted in a definite clinical picture. If the water and salts are restored, the condition should be ameliorated. Our practical results have not been quite as good as we had hoped.

Bicarbonate of soda administered intravenously in some cases has given amazing results. In other cases it was followed by improvement that was discouragingly temporary, and frequent injections were required.

We have found it more difficult to increase the blood chlorides. In some cases in which the patient was receiving saline solution subcutaneously and intraperitoneally, there was no increase in blood chlorides, and at times there was actually a decrease.

In a number of cases the blood chlorides were brought to a normal level by these means, but at no time did we succeed in increasing the blood chlorides above normal with a consequent decrease in base bicarbonate, as Dr. Hartmann has. However, Dr. Hartmann has used Ringer's solution, and we have used saline solution.

In some cases we have effected a normal blood chemical value and have maintained it within normal limits, but the patients have died.

Is another salt necessary? The fact that Dr. Hartmann has gotten better results with Ringer's solution than we have with saline solution might be of significance.

It is possible that the organs of the body have undergone such severe damage because of the disturbances in water and mineral metabolism that reparation is impossible. However, if such is the case, better results should be obtained with patients who were admitted to the hospital early in the course of the disease. We have not found this to be so.

Dr. Marriott suggests histamine as an etiologic factor. Histamine, tyramine, and their companion amines have been blamed so extravagantly for so many ills that they have rather lost repute with chemists. It is known that histamine is a normal constituent of the human intestine. It is known that large quantities of it taken by mouth have proved innocuous in experimental animals. This occurs in normal intestines, but in experimental obstruction and damage to the intestines, no absorption of histamine has been found.

Clinically the pictures are similar, but after all both merely present a state of shock. Anaphylactic shock is similar. In this connection, it is of interest that a number of our patients developed diarrhea on weaning. In still others the intoxication began coincident with their removal from home to a nursery where they probably received somewhat different food.

Chemically, there are points of resemblance in histamine shock and intestinal intoxication. Common to both is the concentration of the blood and retention of nitrogenous products. A decrease in blood chlorides is more constant in histamine shock than in intestinal intoxication. In histamine shock there is a great increase in blood sugar due supposedly to its action on epinephrine. We have not found this in intestinal intoxication. We have found a slight increase in blood sugar initially due to concentration but a rapid return to normal on administration of fluids. Has Dr. Marriott some specific chemical reasons for suggesting histamine? Has he made any examination of the liver to see if there was absence of glycogen? Has he found an increase in blood platelets which have been reported in histamine shock? Has he made any test in the blood serum, either colorimetric or biologic? Has he examined the urine for the presence of imidazol acetic acid?

Dr. Lynne A. Hoag: Dr. Marriott and his collaborators have made important contributions to the study of diarrhea and dehydration not only so far as the etiology is concerned but regarding the profound physical and chemical changes that occur in the body. The latter have been lucidly presented by Dr. Hartmann. He emphasized the importance of rising plasma concentration with the accompanying relation to the development of acidosis. He also issued a warning against the use of sodium chloride in these oliguric patients. The potential danger of

such treatment is supposed to be the ability of sodium chloride further to increase the acidosis.

Data from our clinic show results at variance with those of Dr. Hartmann as far as the use of sodium chloride clyses is concerned. This difference may hinge on the varying activity of the kidneys of the patients under observation in the two series. In Dr. Hartmann's series, it is implicitly acknowledged that oliguria persisted during treatment. Since it is well recognized that oliguria and anuria are perhaps the most important factors in the development of acidosis in dehydrated infants, it is important to realize this fact. Indeed, the question of oliguria does not receive the attention that it merits in directing the treatment for acidosis occurring during the course of dehydration. This is fully as important a factor as the changes in fluid content of the tissues and is of perhaps much greater importance as far as the immediate results of treatment are concerned. Excluding moribund patients, the failure to produce and maintain diuresis by the administration of parenteral fluids is proof that the quantity of fluid offered that particular patient is insufficient.

Dr. Schloss has recognized this fact, and since about 1912 it has been the practice in his clinic to induce as rapidly as possible a distinct diuresis and attempt to maintain it. This can be accomplished in any patient who lives even two or three hours after treatment. It is felt that diuresis is much more readily accomplished when the saline clyses are combined with the intravenous injection of hypertonic dextrose solutions. The number of such combined treatments given is decided, to a considerable degree, on the basis of the presence or absence of satisfactory restoration of kidney function as measured clinically by the amount of diuresis.

Allow me to illustrate with selected typical examples from thirteen patients who have been carefully studied in the wards of the New York Nursery and Child's Hospital. These cases showed, in general, a lesser degree of severity than those previously reported by Dr. Hartmann (Am. J. Dis. Child. **35**:557 [April] 1928). This is evidenced by the fact that four of our thirteen patients died, whereas eleven of Dr. Hartmann's thirteen patients whose conditions were fully studied, succumbed.

The data presented on the lantern slides can be summarized as follows: Only three patients showed any tendency toward an increasing concentration of chlorine in the serum following the injections of large amounts of saline clyses. Even then only one showed at the same time a decrease in the bicarbonate reserve. The other ten patients all showed falling concentrations of chlorine and rising concentrations of carbon dioxide. It is interesting to note that in six of these patients urine and stool collections were secured at eight different periods. From the data so secured, it was found that the minimum urine volume in any one period was 200 cc. in twenty-four hours. The maximum volume was 520 cc., and the average for all the periods was 315 cc. in twenty-four hours. When one remembers that the patients varied in weight from about 6 to 13 pounds (2.7 to 5.9 Kg.), it is easy to see that these quantities mean a high rate of urine output.

Dr. Hartmann has advised the more frequent use of sodium bicarbonate in the treatment for the acidosis of dehydration. I feel strongly that the real indication for the use of a fixed alkali of this nature is the presence not only of a low carbon dioxide concentration but the simultaneous observation of a low total fixed base in the plasma. This was found in only one patient of the series, and the information was not available until after the patient had died. It seems to me that, in view of the fact that diuresis can be produced with such rapidity by the active administration of parenteral fluids and that this restoration of kidney function will in itself tend rapidly to readjust the acid base status of the blood, there is little theoretical indication for the use of sodium bicarbonate.

The statement that the neutral sodium chloride may produce acidosis seems paradoxic. One must remember, however, that a similar action has been proved for neutral calcium chloride. The explanation offered for this seeming paradox is that the total base of the body shows a proportionately greater loss in diarrheal stools than in normal stools. Dr. Hartmann cited as evidence for this the analysis

of normal and diarrheal stools by Dr. Holt and his collaborators in 1915. When I examined Dr. Holt's figures closely, I found that the excretion of total fixed acid in the stools rises in the same proportion and that the relation of total fixed acid to total fixed base remains surprisingly constant throughout the rising daily volume of stool.

I must also call attention to the fact that the excretion through the urine is totally neglected in his data. When the figures secured from the analysis of both stools and urine in two normal patients are examined, it is found that the base exceeds the acid by 1.5 times. With this as a rough normal standard, it is interesting to state that in eight periods in six diarrheal patients undergoing treatment with large quantities of saline solution, total fixed base exceeded total fixed acid by an average proportion of only 1.35. Other factors which complicate the ease with which Dr. Holt's figures can be interpreted are: first, the inability to know how much food was unabsorbed in the intestine and how much this unabsorbed food present in the feces may have influenced the relation between the base and the acid; second, the fact that the excretion of organic acids carrying with them definite quantities of fixed base escaped detection in the urine and stool when fixed acids only are being analyzed. It seems, therefore, that in view of these difficulties, one should be cautious in forming a theory concerning the relative rate of excretion of fixed acid and base from the body in diarrhea. I hope to secure further data on this particular problem.

In summary, let me state simply that in a series of thirteen patients suffering from diarrhea and dehydration of average severity, the routine and active use of sodium chloride clyses did not, so far as could be determined, contribute to an increasing acidosis when a satisfactory degree of diuresis was produced and maintained.

Dr. Oscar M. Schloss: Within the past decade it has become apparent that some relationship exists between parenteral infections and infantile diarrhea. I find it difficult to discuss Dr. Marriott's results on the basis of my own experience, for his observations were conducted in a different way from mine, which renders comparison difficult. This applies especially to his second group of cases in which evidence of infection of the middle ear was extremely slight until the mastoid was opened.

Dr. James Wilson has found records of fifty-one postmortem examinations in cases of diarrhea and dehydration for the past four years at the New York Nursery and Child's Hospital. In thirty-nine of these cases, pus was found in the middle ear and the mastoid antrum. In no case was a true mastoiditis with involvement of the bone present.

Dr. Rogers has collected the clinical statistics from 1926 to 1928, inclusive, which comprise 175 cases of dehydration and diarrhea. Only 82 of these, 47 per cent, showed a history of otitis media before the diarrhea. There were 17 cases, however, in which infection of the middle ear developed during the course of the disease. Our results merely permit us to conclude that otitis media accompanies diarrhea but offer no proof that the infection of the ear is a definite causative factor.

There is much evidence against Dr. Marriott's views. Diarrhea is not a common symptom of clinical mastoiditis. Otitis media, which is always accompanied by pus in the mastoid antrum, is an extremely common disease and is rarely accompanied by severe diarrhea. The mastoid antrum and middle ear of infants are exceedingly small, and a toxin must be extremely powerful and absorption very active to cause the severe symptoms of "intestinal intoxication."

Despite all theoretical objections, it would seem that the proof of Dr. Marriott's view must rest on a therapeutic test. If he can show that by early operation on the mastoid antrum the mortality from diarrhea is substantially less than by other methods, it will go a long way toward proving his view.

As nearly as I could judge from Dr. Marriott's charts, the mortality in the cases of diarrhea and dehydration was about 58 per cent. Powers observed a mortality of about 35 per cent in patients treated by repeated injections of saline

solution and by frequent transfusions. Statistics for 1921 and 1922 collected by Dr. Hood and Anderson showed a mortality of 40 per cent in 100 severe cases.

In a more recent series of 175 reports of severe or moderately severe cases collected by Dr. Rogers, the mortality was 34.4 per cent. One can only conclude that the results obtained by operation on the mastoid are, to say the least, no better than have been obtained by more conservative methods.

It has been known for many years that severe diarrhea leads to depletion of water in the organism. It was not appreciated, however, to what a marked degree such depletion occurred, and treatment consisted in the administration of an occasional hypodermoclysis of saline solution.

Following the work of Howland and Marriott, attention was focused on the acidosis which they demonstrated in severe diarrhea. Treatment was directed toward the acidosis, and the attempt was made to correct this by intravenous injections of large amounts of 4 per cent bicarbonate solution. The results were not encouraging, and in many instances these large amounts of bicarbonate were definitely harmful. About this time, Dr. Harrington and I became convinced that the most serious result of dehydration was the suppression of urine. We found that the concentration of the blood, high blood chloride, the increased nonprotein nitrogen and the severe acidosis disappeared once the secretion of urine became established. The best means of accomplishing this we found to be the administration of large amounts of physiologic solution of sodium chloride or Ringer's solution and the intravenous injection of hypertonic dextrose solutions. By such procedures, we have frequently observed a plasma bicarbonate of from 12 to 15 per cent by volume become normal or nearly normal within from twelve to eighteen hours. Unless urine is secreted, death occurs quickly. In addition to the use of saline and dextrose solutions, frequent transfusions are of value.

I have therefore seen no harmful effect from the administration of sodium chloride in patients with dehydration provided urine is secreted. It is probable that in the presence of oliguria acidosis may be increased by the injection of sodium chloride. But the secretion of urine can be reestablished in practically every case, and in this event acidosis rapidly decreases. I have observed a number of infants with 700 mg. of chlorine as sodium chloride in 100 cc. of blood on admission to the hospital, but the chloride rapidly became normal when sufficient saline and dextrose solutions were administered to cause diuresis.

The use of sodium bicarbonate as advocated by Dr. Hartman may be of some value, but one can hardly consider the indication urgent unless there is a diminution of total base in the blood, which rarely occurs. Moreover, once the secretion of urine is established the acid base balance becomes normal, and unless urine is secreted bicarbonate can be of little more than the most temporary value.

DR. CHARLES HENDEE SMITH: We are all indebted to Dr. Marriott for calling attention to the value of simple antrotomy. For years, a number of small infants had mastoid infections complicated by gastro-enteritis. Formerly, the otologists would not operate, because the general condition did not permit the old complete operation. Since Dr. Marriott first reported the results in these cases, it has been possible to get the otologists to do the simple operation under local anesthesia, removing a simple button; many lives have thus been saved.

Whether most diarrheas are due to mastoid infection, I am not sure, but there are certainly more of such cases than has been realized.

As far as the administration of fluids is concerned, Dr. Schloss's statement that too much cannot be given is important. A recent incident in the wards illustrates the fallacy of the parenteral method at times. An intern had given a clysis of approximately 150 cc. It was noted by another intern that the child had just taken and retained 8 ounces (236 cc.) of water by mouth, nearly twice as much as the clysis.

DR. MARRIOTT: The question has been raised as to whether or not histamine is responsible for the symptoms observed in cases of "alimentary intoxication." Under normal conditions, histamine introduced into the gastro-intestinal tract is relatively harmless. It appears to be detoxicated in passage through the intestinal

mucosa or else in the liver. On the other hand, histamine introduced parenterally is capable of producing considerable harm and bringing about certain of the symptoms observed in these infants. It has been suggested, and there is certain evidence to support the belief, that histamine may be absorbed from the injured intestinal mucosa. Organisms isolated from the intestinal tract of some of the infants with mastoid involvement were shown to be histamine producers. I have not, as yet, attempted to obtain evidence of histamine in the circulating blood nor have I examined the livers of these infants for glycogen content. I consider the observation that the organisms found in the mastoid were histamine producers of possible significance.

Infection may influence nutrition in a variety of ways, as has been well recognized for years. In young infants, the symptoms of infection are more likely to be connected with the gastro-intestinal tract. The ears are only one place in which the infection may be present, and they are not the only place. The mastoid antrums are doubtless involved in most cases of otitis media, but are adequately drained by simple paracentesis. It is only in those young infants in whom the embryonal mucosa swells sufficiently to block off the antrum that post-auricular drainage becomes necessary. The symptoms produced will depend a great deal on the type of infection present. Organisms which lead to typical mastoid disease with swelling, redness and subperiosteal abscess do not appear to produce the same type of gastro-intestinal and nutritional disturbances as some other organisms which remain latent in the antrum. In the series reported, none of these frank mastoid cases have been included. The mortality was low in this group, not more than 10 or 15 per cent. All infants with evidences of infection of the mastoid antrum who were operated on, some when obviously in the terminal stages, have been included in the series. The mortality does not represent the mortality of the entire group of cases of athrepsia or "alimentary intoxication." If all cases are included, the mortality is distinctly lower, about 16 to 20 per cent. The group described includes those infants many of whom would, I believe, succumb except for drainage of the infected focus.

In all cases every effort was made to control the vomiting and diarrhea by thick cereal feeding when vomiting was a prominent symptom, and I have not hesitated to use opiates for the control of the diarrhea. Operation alone, feeding alone, or the administration of blood, fluid and alkali is not sufficient to bring about cure in these cases. Every means must be used, and the indications must be met as they arise.

DR. HARTMANN: Replying to Dr. Sullivan's remarks in regard to the point that alkali had to be administered repeatedly, and that after all the acidosis was really due to a secondary symptom such as diarrhea, and her inquiry as to why something was not done to stop the vomiting and diarrhea: I do try to stop the vomiting and diarrhea. When we think the vomiting and diarrhea are due chiefly to mastoid infection, we drain the mastoids, supporting the patient, however, with adequate amounts of fluid and the right kind of salt until immunity to the infection is established, and the symptoms, vomiting and diarrhea, cease. The amount of repetition of administration of alkali is dependent largely on the time required for the establishment of immunity.

I fully agree with Dr. Hoag. I tried to show that the amount and type of urinary secretion were extremely important in determining the effects of administration of salt solution. I have said emphatically that the danger of administration of salt solution to infants with dehydration was slight if adequate quantities of urine are secreted. There is no doubt as to the way in which chloride causes excretion of bicarbonate. The earlier work of German authors, particularly that of Gyorgy on the production of salt fever, illustrates this beautifully. Gyorgy did this work before microchemical methods for determination of electrolytes in the blood were developed, and his observations were largely on the urine. He did show, however, that administration of sodium chloride frequently caused the excretion of alkaline urine. More recently, working in our laboratory, Dr. Schoenthal has similarly produced the picture of salt fever, but has observed

changes both in the blood and in the urine and has noted that the oral administration to normal infants of sodium chloride with restriction of water would diminish the plasma bicarbonate by as much as 10 per cent by volume and that the urine would become more alkaline, showing that fixed base had left the blood plasma and entered the urine.

The main objection to the continued administration of salt solution in infants with marked acidosis and dehydration is this: although water is given in a form immediately available, one must wait an appreciable amount of time, as Dr. Schloss said, perhaps fifteen hours, before enough acid bound to ammonia is secreted into the urine appreciably to raise the bicarbonate content of the plasma. In infants dying of acidosis, fifteen hours is a long time to wait, often too long. Why wait fifteen hours to raise an extremely low bicarbonate content through the intermediate effect of urinary secretion when it can be raised effectually and immediately by the administration of sodium bicarbonate itself?

Book Reviews

INVESTIGATIONS CONCERNING THE GOAT'S MILK ANEMIA. By W. GRÄVINGHOFF. Price, 4.80 marks. Berlin: S. Karger, 1928.

The author states that the only certain knowledge concerning the present confusion in regard to the etiology and pathogenesis of "alimentary anemia" is that the injurious substance leading to alimentary anemia has a definite relationship to the type of food consumed and has its origin in the intestinal tract. Almost without exception it is admitted that an anemia due to cow's milk must be associated with a congenital constitutional peculiarity of the body. The question whether the same is true in regard to goat's milk anemia is still under discussion.

A comprehensive discussion of the views advanced, up to the present, as to other factors in the etiology of alimentary anemia of children includes undernutrition, both quantitative and qualitative, with special reference to a deficiency in iron and vitamin and results obtained from iron and vitamin therapy. An explanation of the processes by which iron effects improvement or cure will also furnish important facts about the origin of alimentary anemia. Czerny's theory that the milk has a direct injurious action on the blood, the destructive agent being especially related to the fat, is discussed with special reference to the action of the fatty acids. That destruction of blood is an outstanding characteristic of alimentary anemia, especially goat's milk anemia, is the contention of some investigators who base their conclusions on the rather common discovery of urobilin in the stools, and occasionally a hematinemia. Such evidence of hemolysis must be constant in order to prove the theory that the fatty acids cause the anemia by direct action on the red blood cells. This has not yet been proved.

Goat's milk anemia progresses more rapidly and to a more severe degree than cow's milk anemia. It is also less dependent on a congenital inferiority of the body for its occurrence. It may simulate any form of alimentary anemia but differs from cow's milk anemia in that it is possible for it to progress to a form simulating an aplastic anemia. Goat's milk anemia is further distinguished from cow's milk anemia by the following clinical observations made in certain cases: disturbances of protein metabolism, bilirubinemia, hematinemia, increased urobilinogenuria, a decrease in erythrocyte resistance, that is, increased fragility and failure to respond to otherwise effectual therapy.

Reports of autopsies in children with goat's milk anemia are few, and most of those reports are rather incomplete. The author discusses at length the changes in bone marrow occurring in different types of anemia. He stresses the point that in adults the reaction of the bone marrow to anemia-producing agents is likely to be different from that in infants. Goat's milk anemia may progress to a blood picture closely resembling pernicious anemia, but observations concerning the bone marrow are different. Also in infantile pseudoleukemia the blood picture often resembles that of pernicious anemia, but shows an entirely different change in the bone marrow.

A case is cited in which a child with a blood picture resembling that of an aplastic anemia showed, at autopsy, changes in the bone marrow and in the spleen much like those found in pernicious anemia. These observations would seem to show that a close relationship exists in the anatomic observations as well as in the clinical manifestations, between goat's milk anemia and the severe anemias of adults; in each case some powerful toxic noxa in conjunction with a constitutional peculiarity is responsible for the disease. Possibly a better knowledge of the pathogenesis of any of these severe anemias will bring about a clearer knowledge of goat's milk anemia and of the whole group of alimentary anemias.

Experiments on young dogs proved that they have a physiologic anemia that persists even to the third month of life and that when fed on goat's milk the degree of this physiologic anemia is considerably increased; also that the physiologic

return to normal which regularly takes place in dogs on their usual ration of food was definitely hindered by goat's milk. The cause of this influence of goat's milk seemed to be in an interference with the normal activity of the bone marrow, rather than in a destruction of red blood cells.

DER INTESTINALE INFANTILISMUS UND ÄHNLICHE FORMEN DER CHRONISCHEN VERDAUUNGSSTÖRUNG. Beiheft No. 21 of Jahrbuch für Kinderheilkunde. By A. FANCONI, M.D., Department of Pediatrics, University of Zurich, Switzerland. Price, 11 R. M. Pp. 202, with 42 illustrations. Berlin: S. Karger, 1928.

This volume is not a monograph, but represents the results of careful study of forty-five cases of celiac disease and thirty-five cases of other chronic intestinal disorders in young children treated during the past seventeen years. In 1923, Hablützel-Weber had already reported on twenty-five of the celiac diseases. As many of the patients remained in the hospital for months or years, opportunity was afforded for prolonged and detailed observations on various phases of this baffling syndrome. Studies of fat, protein, carbohydrate and mineral metabolism were made, also determinations on the acid-base equilibrium, chemical analyses of the blood, blood counts and influence of intercurrent fevers on metabolism. A number of the patients were subjected to roentgen examination of the intestinal tract and of the bones. The former showed gastric retention after eight hours and intestinal distention, the latter an osteoporosis in several of the most chronic cases. Numerous clinical observations were made on such complications as intercurrent rickets, scurvy, tetany and genito-urinary infections. Little work was done on the bacteriology of the feces, and nothing is offered in regard to etiology or prophylaxis.

Fanconi is much less pessimistic about prognosis than were Lehndorff and Mautner in their recent monograph on celiac disease. The bibliography is overwhelmingly German, with but one English and one American reference. Howland's epochal work on treatment is not mentioned. In no instance was the three-phased high-protein diet used. No two of the forty-five patients were fed alike, i. e., there is no attempt at standardization of treatment. In recent years Professor Feer, director of the clinic, has tried a fruit and vegetable diet enriched with cottage cheese, buttermilk, powdered skimmed milk and liberal portions of lean meat. The acidity of the fruit is neutralized by the addition of precipitated chalk. Many of the patients develop diarrhea, and some lose weight during the first weeks or months. Gains in weight seldom occur without the addition of proteins. Through the laxative action of the diet, the abdominal distention and intestinal stasis are reduced. The finely puréed vegetables have a beneficial action on the anemia.

About half of the volume is devoted to detailed case histories. There are twelve excellent photographs of patients, nine x-ray pictures of the intestine and bones, twenty-six tables and twenty-eight charts. This wealth of data represents years of labor and should prove interesting and valuable to students of this unique disease of unknown etiology.

KINDERHEILKUNDE UND PFLEGE DES GESUNDEN KINDES. By E. NOBEL and C. PIRQUET. Price, 8.60 marks. Pp. 276, with 77 illustrations. Berlin: Julius Springer, 1928.

In the midst of a life rich with scientific research, Dr. Clemens Pirquet has found time to write for the semilaity a book called "Kinderheilkunde und Pflege des Gesunden Kindes." This book of which Dr. E. Nobel is co-author is a sort of a compendium of the diseases of children for sisters and nurses. It is written in an informal and lucid style and is easy to understand.

Its only drawback is its completeness, which necessitates brevity and, therefore, results in inadequate explanations, when more complete information might be desirable.

The authors have attempted to cover almost the entire field of pediatrics, the care of the well infant as well as the diagnosis and treatment of disease in the

sick. In part I they discuss the physiology and pathology of the new-born, his physical and mental development and his daily care. Part II is devoted to the nutrition of children, beginning with the chemistry of foods and ending with the preparation of specific dishes for smaller and older children. In part III psychic abnormalities in childhood are touched on.

In the chapter on nutrition there are many important recipes for older as well as preschool children. These foods are different in quality and taste from our American dishes and may therefore be of value in the dietary of children suffering from poor appetite.

The chapter on psychic and emotional disturbances is up to date in its point of view and gives proper consideration to the modern principles in child psychiatry. Attention is paid to the influence of the social status and the occupation of the parents, the psychologic make-up of the parents and their influence on the physical and emotional health of the child.

Several chapters are of special interest; for instance the chapter on the relation between heredity and environment as they affect the child in disease. The authors take sides somewhat with the eugenists, although they admit that environment plays some rôle in the production or rather the aggravation of symptoms.

Their frank and unexaggerated explanations and their admission that there are still some disputed questions in pediatrics are especially gratifying to one who in the last year had reviewed books with the same subject matter yet with less careful consideration of the truth.

The book is packed with important facts and deserves translation into English.

LEHRBUCH DER KINDERKRANKHEITEN. By HEINRICH LEHNDORFF, M.D. Price, 12 R.M. Pp. 330. Vienna: Julius Springer, 1928.

This is a textbook of pediatrics written in easily readable German, which avoids the cumbersome, involved sentences so frequently met in this language. The book follows closely the usual technic of presentation, but an innovation is found in the short preamble heading each division. In this preamble, the anatomic differences in the child as compared with the adult and methods of examination used in children are fully discussed.

The main divisions of the book are based on the systems of the human body, to which are added a section on infectious diseases and one on the diseases of the new-born. It is pleasing to note that the section on disturbances of nutrition is completely separated from that on diseases of the digestive tract.

The therapy and medication can hardly prove useful to physicians practicing in countries not supplied by the pharmaceutical houses of Central Europe. In fact, the entire book ignores the advances of pediatric study in other languages. It is definitely stated that the use of artificially soured milk (lactic acid, citric acid) has not gained foothold in practice. Other standard texts of pediatrics cover the ground as thoroughly.

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CENTRAL STATES PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 120 E. Wisconsin St., Milwaukee.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Ave., Chicago.
Place: Milwaukee. Time: October, 1929.

SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

Chairman: Dr. E. C. Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. J. Waring, De Renne Apts., Savannah, Ga.
Place: Miami, Fla. Time: Nov. 20-22, 1929.

LOCAL

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. W. L. Channell, Medical Bldg., Oakland.
Secretary: Dr. J. E. Parrott, Medico-Dental Bldg., San Francisco.
Place: Various Teaching Schools. Time: Monthly.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. George P. Laton, 1136 W. 6th St., Los Angeles.
Secretary: Dr. William Sidney Bowers, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Elsie Seelye Pratt, Republic Bldg., Denver.
Secretary and Treasurer: Dr. Wilford W. Barber, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month, 2:30 p. m., September to May, inclusive.

GEORGIA PEDIATRIC SOCIETY

President: Dr. W. N. Adkins, Medical Arts Bldg., Atlanta.
Secretary and Treasurer: Dr. E. N. Gleaton, 212 E. Gaston St., Savannah.

PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

Chairman: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Secretary: Dr. William Kiser, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St., Atlanta. Time: Second Thursday of each month from October to April, at 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Edwin T. Wyman, 483 Beacon St., Boston.
Secretary-Treasurer: Dr. Randolph K. Byers, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Maurice Blatt, 185 N. Wabash Ave., Chicago.
Secretary: Dr. J. K. Calvin, 104 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. L. R. De Buys, 1417 Delachaise St., New Orleans.
Secretary-Treasurer: Dr. C. T. Williams, 7401 Burthe St., New Orleans.

DETROIT PEDIATRIC SOCIETY

President: Dr. M. Boyd Kay, 10 Peterboro St., Detroit.
Secretary: Dr. Charles A. Wilson, 71 E. Ferry St., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. Ray Shannon, Lowry Bldg., St. Paul.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester, Minn. Time: Winter, Spring, Summer, Fall.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Park J. White, Beaumont Bldg., St. Louis.
Secretary-Treasurer: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

NEBRASKA-IOWA PEDIATRIC SOCIETY

President: Dr. Floyd Clarke, City Nat'l Bank Bldg., Omaha.
Secretary: Dr. R. B. Eldredge, Medical Arts Bldg., Omaha.
Place: Add-Sell Restaurant. Time: Second Thursday of each month from October to May, inclusive, 6 p. m.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Louis M. Ruderman, 961 Eastern Parkway, Brooklyn.
Secretary: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

BRONX PEDIATRIC SOCIETY

President: Dr. William Hinz, 1964 Grand Concourse, New York.
Secretary: Dr. L. H. Barenberg, 1749 Grand Concourse, New York.
Place: Concourse Plaza, 161st St. and Grand Concourse, New York. Time: Second Wednesday of each month, except June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various Cities in New York. Time: Fourth Thursday of October, January and April.

PEDIATRIC SECTION OF THE NEW YORK ACADEMY OF MEDICINE

President: Dr. Stafford McLean, 17 E. 71st St., New York.
Secretary: Dr. F. Elmer Johnson, 300 West End Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester, N. Y.
Secretary: Dr. Edwin R. Reynolds, 1620 St. Paul St., Rochester, N. Y.
Place: Arranged by Program Committee. Time: First Friday of each month from October to May.

THE PEDIATRIC SECTION OF THE ACADEMY OF MEDICINE OF CLEVELAND

Chairman: Dr. C. W. Wyckoff, 8314 Euclid Ave., Cleveland.
Secretary: Dr. C. L. Ruggles, 10616 Euclid Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Ralph M. Tyson, 334 S. 21st. St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22nd St., Philadelphia. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Zaccheus R. Scott, Westinghouse Bldg., Pittsburgh.
Secretary: Dr. Theodore C. Elterich, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months.

THE SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. E. A. Hines, Seneca.
Secretary-Treasurer: Dr. R. M. Pollitzer, 105 E. North St., Greenville.
Place: Charleston. Time: May 8, 1929.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. A. G. Quinn, 1193 Madison Ave., Memphis, Tenn.
Secretary: Dr. Kinsey M. Buck, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

TEXAS PEDIATRIC SOCIETY

President: Dr. Edwin G. Schwarz, Medical Arts Bldg., Fort Worth.
Secretary-Treasurer: Dr. Ramsey Moore, Medical Arts Bldg., Dallas.

RICHMOND PEDIATRIC SOCIETY

President: Dr. J. B. Stone, 2042 Park Ave., Medical Arts Bldg., Richmond, Va.
Secretary: Dr. Samuel A. Anderson, Jr., 2326 W. Grace St. Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St., Richmond, Va. Time: First Thursday of each month (other than during the summer).

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Charles E. Conrad, Harrisonburg.
Secretary: Dr. William B. McIlwaine, Petersburg.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. E. D. Carder, 736 Granville St., Vancouver, B. C.
Secretary and Treasurer: Dr. George A. Lamont, 736 Granville St., Vancouver, B. C.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Arthur H. Gray, Lumber Exchange Bldg., Seattle.
Secretary: Dr. Armin Rembe, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, at 7 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. A. L. Kastner, 120 E. Wisconsin St., Milwaukee.
Secretary: Dr. F. R. Janney, 418 E. North Ave., Milwaukee.
Place: Children's Hospital, Milwaukee. Time: Second Wednesday of each alternate month, beginning with February.

PEDIATRIC SECTION, ACADEMY OF MEDICINE, TORONTO

Chairman: Dr. F. R. Hassard, 1361 King St. West, Toronto.
Secretary: Dr. G. A. Davis, 12 Belsize Dr., Toronto.
Time: November 17, December 15, February 16 and March 15.